VERIFICATION OF TRANSLATION

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Dated: April 19, 2001

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AMIDE DERIVATIVES OR SALTS THEREOF

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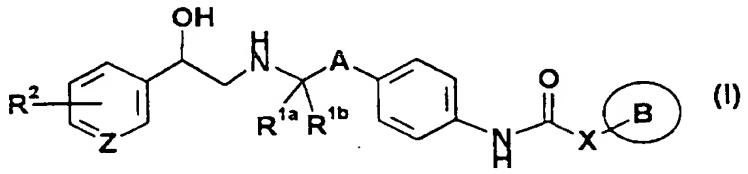
AMIDE DERIVATIVES OR SALTS THEREOF

[Scope of the Claims for Patent]

[Claim 1] An amide derivative represented by the following formula:

[Formula 1]



(In the above formula, each of the symbols means as follows:

ring B: a nitrogen-containing heteroaryl group which may be substituted and may be fused with a benzene ring;

X: a bond, an optionally hydroxy- or lower alkyl-substituted linear lower alkylene, lower alkenylene or carbonyl, or a group represented by a formula -NH- (when X is a linear lower alkylene group which may be substituted with a lower alkyl group, the hydrogen atom bonded to the carbon atom constituting a ring B may form a lower alkylene group together with said lower alkyl group so that a ring is formed);

A: methylene, ethylene or a group represented by a formula $-CH_2O-$;

R^{1a}, R^{1b}: they may be same or different and each is a hydrogen atom or a lower alkyl group;

R^2: a hydrogen atom or a halogen atom; and

Z: a nitrogen atom or a group represented by a formula =CH-)

or a salt thereof.

[Claim 2] A pharmaceutical agent comprising the amide derivative or the salt thereof according to claim 1.

[Claim 3] A therapeutic agent for diabetes mellitus comprising the amide derivative or the salt thereof according to claim 1 as an effective ingredient.

[Detailed Description of the Invention]

[0001]

[Technical Field to which the Invention Belongs]

The present invention relates to pharmaceuticals and, more particularly, it relates to novel amide derivatives or salts thereof and also to therapeutic agents for diabetes mellitus containing them as effective components.

[0002]

[Prior Art]

Diabetes mellitus is a disease accompanied by continuous hyperglycemic state and is said to be resulted by action of many environmental factors and genetic factors. The main controlling factor for blood sugar is insulin, and it has been known that hyperglycemia is resulted by deficiency of insulin

or by excess of factors which inhibit its action (such as genetic cause, lack of exercise, obesity and stress).

Diabetes mellitus is classified into two main types. One is insulin-dependent diabetes mellitus (IDDM) caused by a lowering of insulin-secreting function of pancreas due to autoimmune diseases, and another is non-insulin-dependent diabetes mellitus (NIDDM) caused by a lowering of insulin-secreting function of pancrease due to pancreatic fatigue accompanied by continuous high insulin secretion. 95% or more of diabetic patients in Japan are said to suffer from NIDDM, and an increase in the patients due to a change in daily life style is becoming a problem.

As to the therapy of diabetes mellitus, dietetic treatment, therapeutic exercise and remedy of obesity are mainly conducted in mild cases while, when the disease progresses, oral antidiabetic drugs (for example, insulin secretion promoters such as sulfonyl urea compounds and insulin sensitivity potentiators which potentiate the sensitivity of insulin) are administered. In severe cases, an insulin preparation is administered. However, there has been a brisk demand for creation of the drugs whereby higher control for blood sugar is possible, and development of antidiabetic drugs having a new mechanism and having high usefulness has been demanded.

[0003]

U.S. Patents 4,396,627 and 4,478,849 describe phenylethanolamine derivatives and disclose that those compounds are useful as drugs for obesity and for hyperglycemia. Action of those compounds is reported to be due to a stimulating action to β_3-receptors.

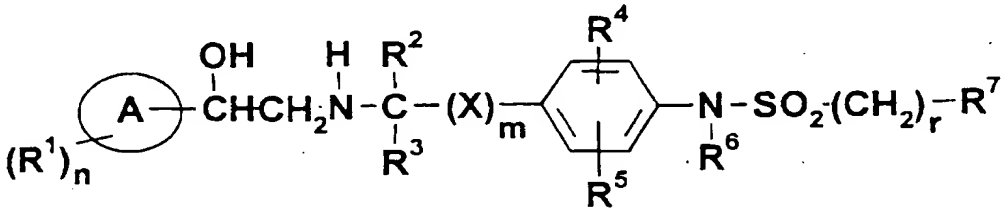
Incidentally, it has been known that β-adrenaline receptors are classified into β_1, β_2 and β_3 subtypes, that stimulation of β_1-receptor causes an increase in heart rate, that stimulation of β_2-receptor stimulates decomposition of glycogen in muscles, whereby synthesis of glycogen is inhibited, causing an action such as muscular tremor, and that stimulation of β_3-receptor shows an anti-obesity and an anti-hyperglycemia action (such as decrease in triglyceride, decrease in cholesterol and increase in HDL-cholesterol).

However, those β_3-agonists also have actions caused by stimulation of β_1- and β_2-receptors such as increase in heart rate and muscular tremor, and they have a problem in terms of side effects. In addition, recently, it was ascertained that β-receptors have differences to species, and it has been reported that even compounds having been confirmed to have a β_3-receptor selectivity in rodential animals such as rats show an action due to stimulating action to β_1- and β_2-receptors in human being. In view of the above, investigations for compounds having a stimulating action which is selective to β_3-receptor in human being have been conducted recently using human cells

or cells where human receptors are expressed. For example, WO 95/29159 describes substituted sulfonamide derivatives represented by the formula set forth below and discloses that due to their selective stimulating action to β_3-receptors in human being, they are useful against obesity, hyperglycemia, etc. However, this patent does not specifically disclose an insulin secretion promoting action and an insulin sensitivity potentiating action of those compounds.

[0004]

[Formula 2]



(In the formula, the symbols should be referred to in the specification of this patent.)

[0005]

[Problems to be Solved by the Invention]

As such, there has been still a demand for creation of therapeutic agents for diabetes mellitus of a new type which have a highly clinical usefulness.

[0006]

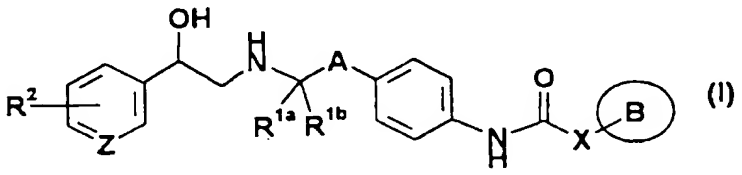
[Means to Solve the Problems]

The present inventors have conducted an intensive investigation on compounds having both an insulin secretion promoting action and an insulin sensitivity potentiating action and found that novel amide derivatives show both a good insulin secretion promoting action and a good insulin sensitivity potentiating action and furthermore show a selective stimulating action to β_3-receptors, leading to accomplishment of the present invention.

That is, the present invention relates to an amide derivative represented by the formula (I) set forth below or a salt thereof, having both an insulin secretion promoting action and an insulin sensitivity potentiating action and further having anti-obesity and anti-hyperlipemia actions due to a selective stimulating action to β_3-receptors. The present invention also relates to a pharmaceutical agent, particularly to a therapeutic agent for diabetes mellitus containing the amide derivative or the salt thereof as an effective ingredient.

[0007]

[Formula 3]



(I)

(In the formula, each of the symbols means as follows:

ring B: a nitrogen-containing heteroaryl group which may be substituted and may be fused with a benzene ring;

X: a bond, an optionally hydroxy- or lower alkyl-substituted linear lower alkylene, lower alkenylene or carbonyl, or a group represented by a formula -NH- (when X is a linear lower alkylene group which may be substituted with a lower alkyl group, the hydrogen atom bonded to the carbon atom constituting a ring B may form a lower alkylene group together with the lower alkyl group so that a ring is formed);

A: methylene, ethylene or a group represented by a formula $-CH_2O-$;

R^{1a}, R^{1b}: they may be same or different and each is a hydrogen atom or a lower alkyl group;

R^2: a hydrogen atom or halogen atom; and

Z: a nitrogen atom or a group represented by a formula =CH-.)

[0008]

[Embodiments of the Invention]

The compound of the formula (I) is further illustrated as follows.

In the definitions used in the formula in this specification, the term "lower" means a linear or branched hydrocarbon chain having from 1 to 6 carbon atoms unless otherwise specified.

Examples of the "lower alkyl group" are methyl, ethyl and linear or branched propyl, butyl, pentyl or hexyl, preferably an alkyl group having from 1 to 4 carbon atoms, and particularly preferably methyl, ethyl, propyl or isopropyl.

Examples of the "lower alkylene group" is a divalent group obtained by removing a hydrogen atom from the above "lower alkyl group", preferably an alkylene group having from 1 to 4 carbon atoms, and particularly preferably methylene, ethylene, propylene or butylene.

[0009]

The term "nitrogen-containing heteroaryl group which may be fused with a benzene ring" in "a nitrogen-containing heteroaryl group which may be substituted and may be fused with a benzene ring" means a ring group where a benzene ring is fused with a heteroaryl group as mentioned later or a non-fused heteroaryl group.

Specific examples of the "ring group where the benzene ring is fused with a heteroaryl group" are fused-ring heteroaryl groups such as quinolyl, isoquinolyl, quinazolinyl,

quinolidinyl, quinoxalinyl, cinnolinyl, benzimidazolyl, imidazopyridyl, benzofuranyl, benzoisoxazolyl, benzoxazolyl, benzothiazolyl, oxazolopyridyl, isothiazolopyridyl and benzothienyl groups; and oxo-added rings such as oxobenzofurayl group.

Examples of the "heteroaryl group" are monocyclic heteroaryl groups such as furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyrazolyl, isothiazolyl, isoxazolyl, pyridyl, pyrimidyl, pyridazinyl, pyrazinyl, thiadiazolyl, triazolyl and tetrazolyl; and bicyclic heteroaryl groups such as naphthylidinyl and pyridopyrimidinyl.

[0010]

The substituent in the "nitrogen-containing heteroaryl group which may be substituted and may be fused with a benzene ring" may be any group which can be usually substituted in this ring group. Preferred examples are a halogen atom and lower alkyl, lower alkenyl, lower alkynyl, hydroxyl, sulfanyl, halogeno lower alkyl, lower alkyl-O-, lower alkyl-S-, lower alkyl-O-CO-, carboxy, sulfonyl, sulfinyl, lower alkyl-SO_2-, lower alkyl-SO-, lower alkyl-CO-, lower alkyl-CO-O-, carbamoyl, lower alkyl-NH-CO-, di-lower alkyl-N-CO-, nitro, cyano, amino, lower alkyl-NH-, di-lower alkyl-N-, and -O-lower alkylene-O- groups.

The "lower alkenyl group" is a linear or branched alkenyl group having 2 to 6 carbon atoms, and its specific examples are vinyl, propenyl, butenyl, pentenyl and hexenyl groups.

The "lower alkynyl group" is a linear or branched alkynyl group having 2 to 6 carbon atoms, and its specific examples are ethynyl, propynyl, butynyl, pentynyl and hexynyl groups.

"Halogen atom" means fluorine atom, chlorine atom, bromine atom or iodine atom, and the "halogeno lower alkyl group" means a group where a hydrogen atom or atoms in the above-mentioned alkyl group is/are substituted with a halogen atom or atoms.

The case when X is a bond means that a carbon atom of the group -CO- is directly bonded to the ring B.

[0011]

The compound (I) of the present invention has at least one asymmetric carbon atom and therefore, there are optical isomers such as (R)-compounds and (S)-compounds, racemates, diastereomers, etc. The present invention includes all and each of isolated isomers and mixtures thereof. The present invention also includes hydrates, solvates (such as those with ethanol) and polymorphic substances of the compound (I).

The compound (I) of the present invention may form a salt with an acid. Examples of the salt are acid addition salts with mineral acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, nitric acid and phosphoric

acid; and those with organic acids such as formic acid, acetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric aid, maleic acid, lactic acid, malic acid, citric acid, tartaric acid, carbonic acid, picric acid, methanesulfonic acid, ethanesulfonic acid and glutamic acid.

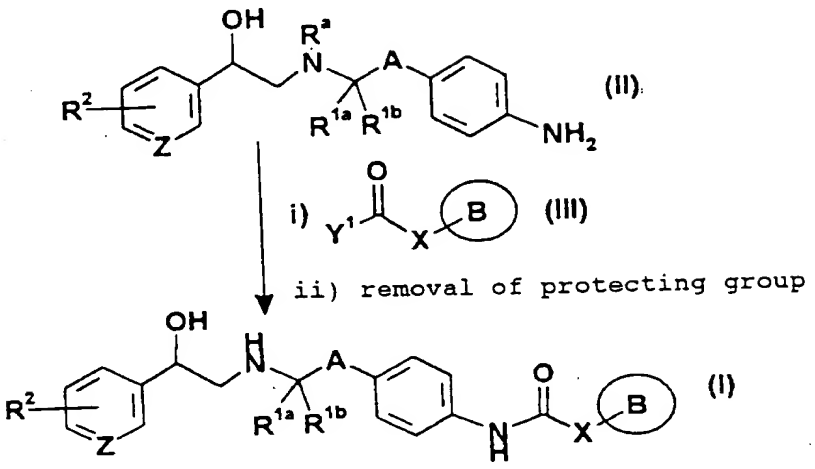
[0012]

(Manufacturing Method)

The compound of the present invention or the salt thereof may be manufactured by application of various synthetic methods utilizing the characteristics of its fundamental skeleton or type of the substituent. Representative manufacturing methods are illustrated as hereunder.

First Manufacturing Method

[Formula 4]



(In the formulae, R^{1a}, R^{1b}, R^2, A, B, X and Z have the same meanings as defined already; R^a is a protective group for amino group; and Y^1 is a leaving group, and more specifically hydroxyl, a lower alkoxy group or a halogen atom.)

[0013]

In this method, the compound (II) and the compound (III) are subjected to amidation, and the protective group is then removed therefrom to synthesize the compound (I) of the present invention.

The amidation in this manufacturing method can be conducted by conventional means.

The solvent may vary depending upon Y^1 of the compound (III) and mostly, an inert solvent or an alcoholic solvent (such as isopropanol) may be applied.

When Y^1 is a hydroxyl group, a method where the reaction is conducted in the above-mentioned solvent in the presence of a condensing agent may be applied. Examples of the condensing agent are N,N'-dicyclohexylcarbodiimide (DCC), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCI), 1,1'-carbonyldiimidazole (CDI), diphenylphosphoryl azide (DPPA) and diethylphosphoryl cyanide (DEPC).

When Y^1 is a lower alkoxy group, a method where the reaction is conducted under heating or refluxing as it is or in the above-mentioned inert solvent may be applied.

When Y^1 is a halogen atom, a method where the reaction is conducted in the above-mentioned inert solvent in the presence of a base may be applied.

[0014]

Examples of the inert solvent are dimethylformamide (DMF), dimethylacetamide, tetrachloroethane, dichloromethane, dichloroethane, chloroform, carbon tetrachloride, tetrahydrofuran, dioxane, dimethoxyethane, ethyl acetate, benzene, toluene, xylene, acetonitrile, dimethyl sulfoxide and a mixed solvent thereof, and they may be appropriately selected depending upon each reaction condition. Examples of the base are inorganic bases such as sodium hydroxide, potassium

hydroxide, sodium carbonate and potassium carbonate; and organic bases such as N-methylmorpholine, triethylamine, diisopropylethylamine and pyridine.

The protective group of the amino group represented by R^a is a protective group which is commonly used for amino group by those skilled in the art, and its representative examples are acyl groups such as formyl, acetyl, propionyl, methoxyacetyl, methoxypropionyl, benzoyl, thienylacetyl, thiazolylacetyl, tetrazolylacetyl, thiazolylglyoxyloyl and thienylglyoxyloyl groups; lower alkoxycarbonyl groups such as methoxycarbonyl, ethoxycarbonyl and tert-butoxycarbonyl groups; aralkyloxycarbonyl groups such as benzyloxycarbonyl and p-nitrobenzyloxycarbonyl groups; lower alkanesulfonyl groups such as methanesulfonyl and ethanesulfonyl groups; aralkyl groups such as benzyl, p-nitrobenzyl, benzhydryl and trityl groups ; and tri-(lower alkyl)silyl groups such as trimethylsilyl group.

[0015]

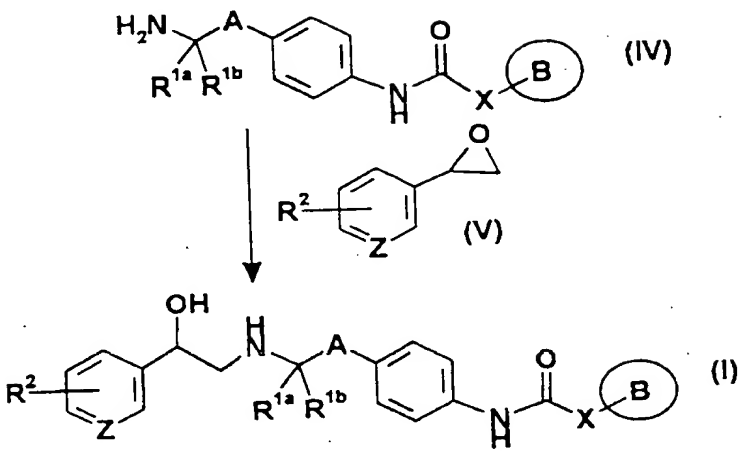
Removal of the protective group in this manufacturing method may be conducted by conventional means. For example, the protective group for the amino group represented by R^a may be easily removed, for example, by i) a method where in case that the protective group is benzhydryl, p-methoxybenzyl, trityl, tert-butoxycarbonyl, formyl, etc., treatment with an acid such as formic acid, trifluoroacetic acid, a mixture of

trifluoroacetic acid and anisole, a mixture of hydrobromic acid and acetic acid, a mixture of hydrochloric acid and dioxane, etc. is conducted; ii) a method where in case that the protective group is benzyl, p-nitrobenzyl, benzhydryl, trityl, etc., catalytic reduction using palladium-carbon or palladium hydroxide-carbon is conducted; and iii) a method where in case that the protective group is a tri-(lower alkyl)silyl group or the like, treatment with water, fluoride anion (tetra-n-butylammonium fluoride, sodium fluoride, potassium fluoride or hydrofluoric acid), etc. is conducted.

[0016]

Second Manufacturing Method

[Formula 5]



(In the formulae, R^{1a}, R^{1b}, R^2, A, B, X and Z have the same meanings as defined already.)

[0017]

In this manufacturing method, the compound (IV) is reacted with the compound (V) to give the compound (I) of the present invention.

The amine compound (IV) and the compound (V) are reacted with each other under heating or refluxing for 1 to 24 hours as they are or in an inert solvent, to give the compound (I) of the present invention.

Examples of the inert solvent are acetonitrile, tetrahydrofuran, 2-butanone, dimethyl sulfoxide and N-

methylpyrrolidone. In the reaction, a base such as sodium bicarbonate, potassium carbonate or diisopropylethylamine may be added to the reaction mixture.

[0018]

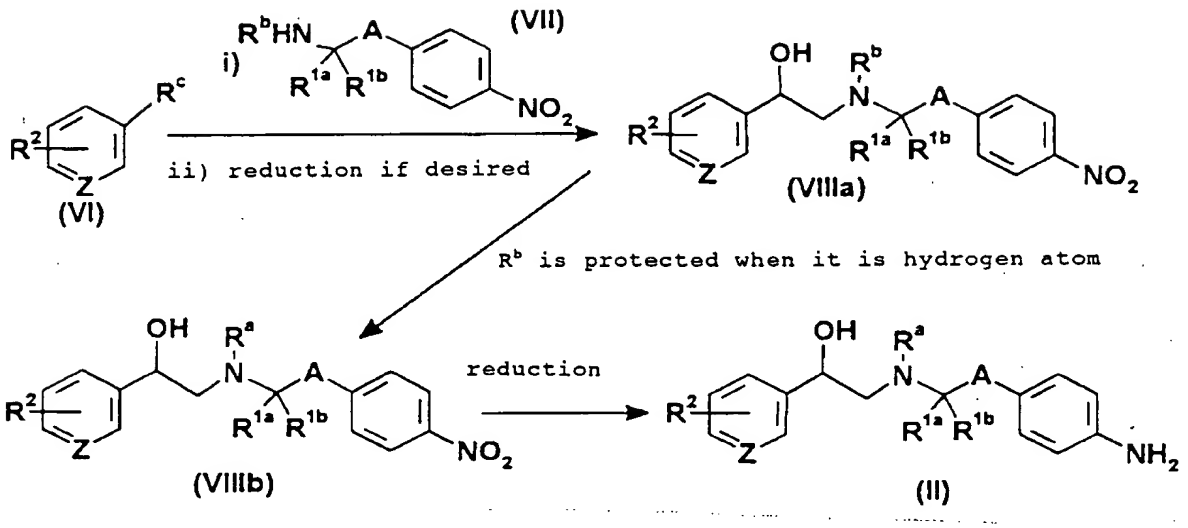
Incidentally, in the above manufacturing methods, it is possible to purify the resulting substance by removing undesired by-products by means of recrystallization, pulverization, preparative thin layer chromatography, silica gel flash chromatography (as mentioned in W. C. Still, et al.; *J. Org. Chem.*, **43**, 2923 (1978)), medium-pressure liquid chromatography and HPLC. The compound produced by means of HPLC can be isolated as a corresponding salt.

The starting material used in the above-mentioned manufacturing methods may be easily manufactured by the methods which are known to those skilled in the art. One of the representative methods is shown as hereunder.

[0019]

(Manufacturing Method for the Starting Compound (II))

[Formula 6]



(In the formulae, R^{1a}, R^{1b}, R^2, A and Z have the same meanings as defined already; R^b is hydrogen atom or a protective group of an aralkyl type for the amino group; and R^c is epoxy, 2-haloacetyl or 1-carboxymethan-1-ol group.)

[0020]

This manufacturing method is composed of from step (a) to step (c) in which the step (a) is a step where the compound (VI) is reacted with the compound (VII), followed by subjecting to reduction to give the compound (VIIIa) depending upon the type of R^c,; the step (b) is a step where protection is conducted when R^b of the compound (VIIIa) is hydrogen atom; and the step

(c) is a step where a nitro group is reduced to an amino group to give the compound (II).

Examples of the protective group of an aralkyl type for the amino group used in the above manufacturing method are benzyl, p-nitrobenzyl, benzhydryl groups, etc.

[0021]

Step (a):

Illustration is made for the following three cases.

1) When R^c is an epoxy group, the compound (VI) may be reacted with the compound (VII) by the same manner as in the above-mentioned second manufacturing method. Reaction conditions such as reaction temperature, solvent, etc. are the same as well.

2) When R^c is 2-haloacetyl group, the compound (VI) is reacted with the compound (VII) in the presence of a base, followed by subjecting to reduction to prepare the compound (VIIIa). The base is the same as that mentioned in the first manufacturing method. The reduction may be conducted in the above-mentioned inert solvent or in a solvent of an alcohol type with stirring in the presence of a reducing agent. Examples of the reducing agent are sodium borohydride, sodium cyanoborohydride, lithium aluminum hydride and borane.

3) When R^c is 1-carboxymethan-1-ol group, the compound (VI) is reacted with the compound (VII) in the presence of a condensing agent, followed by subjecting to reduction in the

same manner as in 2) to prepare the compound (VIIIa). The condensing agent is the same as that mentioned in the first manufacturing method.

[0022]

Step (b):

When R^b in the compound (VIIIa) is hydrogen atom, the amino group is protected by conventional means using, for example, di-tert-butyl dicarbonate or the like, to prepare the compound (VIIIa).

Step (c):

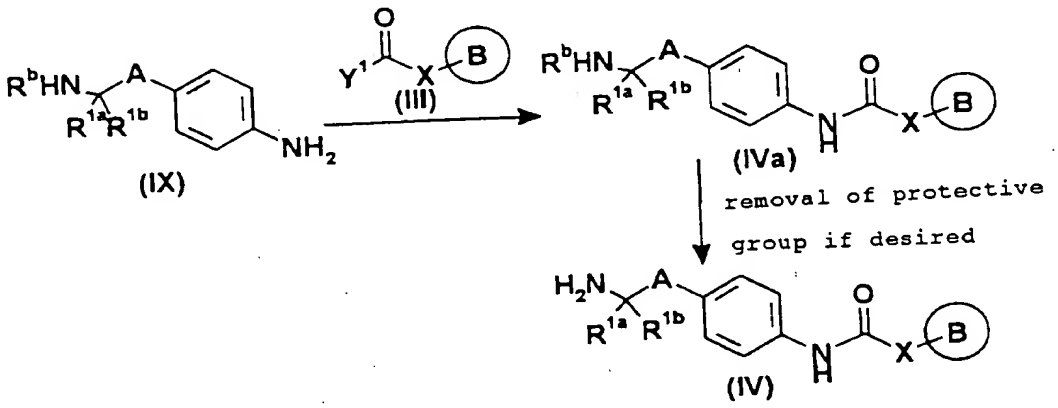
A method for the reduction of nitro group to amino group may be conducted by conventional means such as metallic reduction using iron, zinc, etc. and catalytic reduction using a catalyst such as palladium-carbon, palladium hydroxide-carbon, Raney nickel, etc. R^a becomes hydrogen atom depending upon the reducing condition, but it may be protected again by conventional means.

[0023]

(Manufacturing Method for Starting Compound (IV))

A)

[Formula 7]



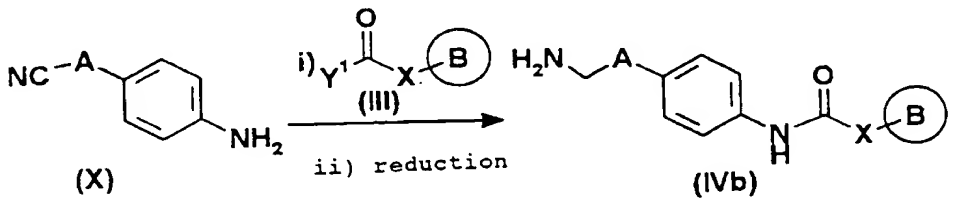
(In the formulae, R^{1a}, R^{1b}, R^b, A, B, X and Y^1 have the same meanings as defined already.)

This reaction is a reaction where the compound (IX) and the compound (III) are subjected to amidation reaction to give a compound (IVa) and, when R^b is a protective group for amino group, the protective group is removed to give a compound (IV). The amidation reaction can be conducted by the same manner as in the above-mentioned first manufacturing method, and the reaction conditions such as reaction temperature and solvent are the same as well.

[0024]

B)

[Formula 8]



This reaction is a reaction where the compound (X) and the compound (III) are subjected to amidation reaction and then to reduction reaction to give a compound (IVa). The amidation reaction can be conducted by the same manner as in the above-mentioned first manufacturing method, and the reaction conditions such as reaction temperature and solvent are the same as well. In the reduction reaction, the above-mentioned catalytic reduction or a method where cobalt chloride and sodium borohydride is used may be applied.

[0025]

With regard to other compounds such as the compound (III), the compound (IV), the compound (V), the compound (VI) and the compound (VII), those which are available in the market or are appropriately synthesized by known methods (such as N-alkylation, cyclization and hydrolysis) from the commercially available compounds may be used.

[0026]

The compound (I) of the present invention which is manufactured as such is isolated and purified as a free compound, a salt thereof obtained by means of salt formation by conventional means, a hydrate, a solvate with various solvents such as ethanol, or polymorphic crystals. The isolation and purification may be conducted by applying common chemical operations such as extraction, concentration, evaporation, crystallization, filtration, recrystallization and various chromatographic means.

Various isomers may be isolated by conventional means utilizing the physico-chemical differences between the isomers. For example, the racemate can be converted to stereochemically pure isomers by common recemic resolution (such as a method where the racemate is changed to diastereomer salts with conventional optically active acid [for example, tartaric acid], followed by subjecting to optical resolution). Incidentally, a mixture of diastereomers may be separated by conventional method such as fractional crystallizaiton or chromatography. In the case of an optically active compound, it may be manufactured starting from an appropriate optically active material.

[0027]

[Effects of the Invention]

The phenethanol derivative of the present invention represented by the formula (I) or the salt thereof has both an insulin secretion promoting action and an insulin sensitivity

potentiating action and also has a selective β_3-receptor stimulating action, so that it is useful as a therapeutic agent for diabetes mellitus.

As confirmed by a glucose tolerance test and a hypoglycemic test in insulin-resisting model animals as described later, the compound of the present invention has both a good insulin secretion promoting action and a good insulin sensitivity potentiating action, so that its usefulness in diabetes mellitus is expected. Although the β_3-receptor stimulating action may have a possibility of participating in expression of the insulin secretion promoting action and the insulin sensitivity potentiating action, other mechanism might also possibly participate therein, and the details thereof have been still unknown yet.

The β_3-receptor stimulating action of the compound of the present invention is selective to β_3-receptors in human being. It has been known that the stimulation of β_3-receptor stimulates decomposition of fat (decomposition of the fat tissue triglyceride into glycerol and free fatty acid), whereby a disappearance of fat mass is promoted. Therefore, the compound of the present invention has an anti-obesity action and an anti-hyperlipemia action (such as triglyceride lowering action, cholesterol lowering action and HDL cholesterol increasing action) and is useful as a preventive and therapeutic agent for obesity and hyperlipemia (such as hypertriglyceridemia,

hypercholesterolemia and hypo-HDL-lipoproteinemia). Those diseases have been known as animus factors in diabetes mellitus, and amelioration of those diseases is useful for prevention and therapy of diabetes mellitus as well.

[0028]

The compound of the present invention is also useful as a preventive and therapeutic agent for other diseases where the improvement of symptom can be achieved by reducing the symptoms of obesity and hyperlipemia such as ischemic coronary diseases (for example, arteriosclerosis, myocardial infarction and angina pectoris), cerebral arteriosclerosis (for example, cerebral infarction) or aneurysm.

Further, the selective β_3-receptor stimulating action of the compound of the present invention is useful for prevention and therapy of several diseases which have been reported to be improved by the stimulation of β_3-receptor. Examples of those diseases are shown as follows.

It has been mentioned that the β_3-receptor mediates the motility of non-sphincteral smooth muscle contraction, and because it is believed that the selective β_3-receptor stimulating action assists the pharmacological control of intestinal motility without being accompanied by cardiovascular action, the compound of the present invention has a possibility of being useful in therapy of the diseases caused by abnormal intestinal motility such as various

gastrointestinal diseases including irritable colon syndrome. It is also useful as the therapy for peptic ulcer, esophagitis, gastritis and duodenitis (including that induced by *H. pylori*), enterelcosis (such as inflammatory intestinal diseases, ulcerative colitis, clonal disease and proctitis).

It is further shown that the β_3-receptor affects the inhibition of release of neuropeptide of some sensory fibers in lung. The sensory nerve plays an important role in neurogenic inflammation of respiratory tract including cough, and therefore, the specific β_3-agonist of the present invention is useful in the therapy of neurogenic inflammation and in addition, has little action to cariopulmonary system.

Moreover, the β_3-adrenaline receptor is capable of resulting in a selective antidepressant action due to stimulation of the β_3-receptor in brain, and accordingly, the compound of the present invention has a possibility of being useful as an antidepressant.

The action of the compound of the present invention has been ascertained to be selective to β_3-receptors as a result of experiments using human cells, and the adverse action caused by other β_3-receptor stimulation is low or none.

[0029]

Effects of the compound of the present invention have been ascertained by the following tests.

1. Hypoglycemic test in kk mice (insulin-resisting model; obesity and hyperglycemia):

Male kk mice (blood sugar level: not lower than 200 mg/dl) were subjected to a measurement of blood sugar level under feeding and then randomly classified into groups. The drug to be tested was compulsorily administered orally or subcutaneously once daily for four days, and the blood sugar level after 15-18 hours from the final administration was compared with that before the administration (n = 6). The blood was collected from a tail vein of the mice using a glass capillary (previously treated with heparin), the protein was removed therefrom, and the amount of glucose in the supernatant liquid (mg/dl) was measured by colorimetric determination by means of a glucose oxidase method.

The compound of the present invention significantly lowered the blood sugar level as compared with that prior to the administration of a comparative drug in both cases of oral and subcutaneous administrations. From this result, it is shown that the compound of the present invention has a good potentiating action to insulin sensitivity.

[0030]

2. Glucose tolerance test in normal rats:

Male rats of SD strain of seven weeks age were fasted for a whole day and night, then randomly classified into groups and subjected to an oral glucose tolerance test (OGTT) (n = 4). The

compound to be tested was administered orally or subcutaneously at 30 minutes before administration of glucose (2 g/kg by oral administration). The blood was collected from an abdominal aorta using a heparin-treated glass syringe from the rats which were anesthetized with pentobarbital (65 mg/kg), the protein was removed therefrom, and the amount of glucose in the supernatant liquid (mg/dl) was measured by colorimetric determination by means of a glucose oxidase method. The insulin value in blood was determined by measuring the amount of insulin in plasma (ng/ml) by means of radioimmunoassay (RIA).

In a group where the compound of the present invention was administered orally or subcutaneously, a significant increase in the insulin value in blood was observed as compared with the group to which no drug was given. An increase in the sugar blood level after administration of glucose was significantly inhibited as well. From those results, it is apparent that the compound of the present invention has a good insulin secretion promoting action and a good hyperglycemia inhibiting action.

[0031]

3. Stimulating test to human β_3-, β_2- and β_1-receptors:

Human β_3-stimulating action was investigated using an SK-N-MC cell system (cells in which human β_3-receptor and human β_1-receptor were permanently expressed were purchased) while human β_2- and β_1-stimulating actions were investigated using a

CHO cell system (cells in which each of human β_2- and β_1-receptors was compulsorily expressed were purchased). Stimulating action of the compound (10^{-10} to 10^{-4} M) were investigated by incubating 10^5 cells/well of each of the cells on a 24-well plate and checking under a subconfluent state after two days using a producing activity of cyclic AMP (cAMP) as an index. Incidentally, the human β_3-stimulating action was investigated in the presence of a β_1-receptor blocker (CGP20712A, 10^{-6} M). Amount of production of cAMP in each cell (pmol/ml) was measured by an RIA method using ^{125}I-cAMP. Intensity of action of each compound was compared by calculating the pD2 value and the maximum activity (I.A. (%) where the maximum reaction of 10^{-6} M isoproterenol was defined as 100%) from the resulting dose-reaction curve.

It has been ascertained that the compound of the present invention has a selective stimulating action to human β_3-receptor.

A pharmaceutical composition containing one or more of the compound of the present invention or the salt thereof as an effective ingredient is prepared using common pharmaceutically acceptable vehicles. Administration of the pharmaceutical composition according to the present invention may be either by oral administration or by parenteral administration by, for example, injection, suppository, subcutaneous agent, inhaling agent or intracystic infusion.

The dose may be appropriately decided depending upon each particular case while taking into consideration symptom, age, sex, etc. of the patient but usually, is around 0.01 mg/kg to 100 mg/kg per day for adults in the case of oral administration, and that is administered at a time or by dividing into 2 to 4 times a day. When intravenous injection is conducted depending upon the symptom, the dose is usually around 0.001 mg/kg to 10 mg/kg per day for adults, and that is administered at a time or by dividing into two or more times a day.

With regard to a vehicle for the preparation, nontoxic solid or liquid substances for pharmaceuticals may be used.

[0032]

Examples of the solid composition for use by means of oral administration according to the present invention are tablets, pills, capsules, diluted powder and granules. In such a solid composition, one or more active substances are mixed with at least one inert excipient such as lactose, mannitol, glucose, hydroxypropyl cellulose, microcrystalline cellulose, starch, polyvinylpyrrolidone, agar, pectin, magnesium metasilicate aluminate and magnesium aluminate. The composition may also contain additives other than the inert excipient such as lubricant (for example, magnesium stearate), disintegrant (for example, calcium cellulose glycolate), stabilizer (for example, lactose) and auxiliary solubilizer (for example, glutamic acid or aspartic acid) by conventional means. Tablets and pills may,

if necessary, be coated with sugar coat such as sucrose, gelatin, hydroxypropyl cellulose and hydroxypropylmethyl cellulose phthalate or with film of gastric or enteric coating substances.

The liquid composition for oral administration includes pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs and contains commonly used inert excipients such as purified water or ethanol. In addition to the inert excipient, the composition may further contain auxiliary agents such as moisturizing or suspending agents, sweeteners, tasting agents, aromatic agents and antiseptic agents.

The injection for parenteral administration includes aseptic aqueous or non-aqueous solutions, suspensions and emulsions. The non-aqueous solutions and suspensions include, for example, distilled water for injection and a physiological saline solution. Examples of the solvent for non-aqueous solution and suspension are propylene glycol, polyethylene glycol, plant oils (such as cacao butter, olive oil and sesame oil), alcohols (such as ethanol), gum arabic and Polysolvate 80 (trade name). Such a composition may further contain auxiliary agents such as isotonizing agents, antiseptic agents, moisturizing agents, emulsifiers, dispersing agents, stabilizers (for example, lactose) and auxiliary solubilizers (for example, glutamic acid and aspartic acid). These may be sterilized, for example, by filtration passing through a bacteria-preserving filter or by compounding of or irradiation

with a bactericide. These may also be used by manufacturing a sterile solid composition, followed by dissolving in sterile water or a sterile solvent for injection before use.

[0033]

[Examples]

The present invention is further illustrated by way of Examples as hereunder. Compounds of the present invention are not limited to those mentioned in the following Examples but cover all of the compounds represented by the above formula (I), salts thereof, hydrates thereof, geometric and optical isomers thereof and polymorphic forms thereof. Incidentally, the case where the material which is used in the present invention is novel is illustrated by way of the following Referential Example.

[0034]

Referential Example 1

Into a solution of 781 mg of 2-pyrazinylacetonitrile in 30 ml of ethanol was passed hydrochloric acid gas at 55°C for one hour. The solvent was evaporated, and the resulting residue was dissolved in ethyl acetate and a saturated aqueous solution of sodium hydrogen carbonate. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated therefrom. The resulting residue was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 1/1) to give 941 mg of ethyl 2-(2-pyrazinyl)acetate.

[0035]

Referential Example 2

To a solution of 1.00 g of ethyl 2-(1H-benzimidazol-2-yl)acetate in 30 ml of acetonitrile were added 812 mg of potassium carbonate and 1.21 g of 4-chlorobenzyl bromide, and the reaction mixture was stirred at room temperature for 15 hours. The mixture was filtered, and the solvent was evaporated *in vacuo* from the filtrate. The resulting residue was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 2/1) to give 464 mg of ethyl [1-(4-chlorobenzyl)-1H-benzimidazol-3-yl]acetate.

[0036]

Referential Example 3

Ethyl 2-(1-benzyl-1H-imidazol-2-yl)acetate hydrochloride (21.4 g) was dissolved in 300 ml of ethanol and 100 ml of tetrahydrofuran, and 4.50 g of 10% palladium-carbon was added to the mixture, followed by stirring for 15 hours in a hydrogen atmosphere under atmospheric pressure. The catalyst was filtered off, and the solvent was evaporated *in vacuo* from the filtrate to give 14.9 g of ethyl 2-(1H-imidazol-2-yl)acetate hydrochloride.

[0037]

Referential Example 4

To 8.80 g of ethyl 2-(1H-imidazol-2-yl)acetate hydrochloride was added 160 ml of 10% hydrochloric acid, and

the mixture was heated to reflux for 50 minutes. The solvent was evaporated *in vacuo* therefrom, and the resulting crystals were washed with 100 ml of acetone and dried to give 6.89 g of 2-(1H-imidazol-2-yl)acetic acid hydrochloride.

[0038]

Referential Example 5

To an ethanolic solution of 1.46 g of ethyl 2-(2-chloropyridin-6-yl)acetate was added 7.5 ml of a 1N aqueous solution of sodium hydroxide at room temperature. The mixture was stirred at room temperature, and 7.5 ml of 1N hydrochloric acid was added thereto. An aqueous solution obtained by evaporation of ethanol was extracted with ethyl acetate. The resulting organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated therefrom to give 1.07 g of 2-(2-chloropyridin-6-yl)acetic acid.

[0039]

The compounds of Referential Examples 6 and 7 were prepared by the same manner as mentioned in Referential Example 5; and the compound of Referential Example 8 was prepared by the same manner as mentioned in Referential Example 4.

Referential Example 6

2-(2-Acetylaminothiazol-2-yl)acetic acid

Referential Example 7

2-(3-Benzyl-2-thioxathiazol-4-yl)acetic acid

Referential Example 8

2-Methyl-2-(2-aminothiazol-4-yl)propionic acid hydrochloride

[0040]

Referential Example 9

To a solution of 1.18 g of guanyl thiourea in 20 ml of methanol was added 1.65 g of methyl 4-chloroacetoacetate. The mixture was heated to reflux for four hours, the solvent was concentrated, and the concentrate was crushed by adding ethyl acetate thereto. The powder obtained by filtering off the solvent was washed with ethyl acetate and dried to give 2.25 g of methyl 2-(2-guanidinothiazol-4-yl)acetate.

[0041]

The compounds of Referential Examples 10 and 12 were prepared by the same manner as in Referential Example 4; and the compound of Referential Example 11 was prepared by the same manner as mentioned in Referential Example 9.

Referential Example 10

2-(2-Guanidinothiazol-2-yl)acetic acid hydrochloride

Referential Example 11

Ethyl 2-[2-(3-fluoroanilino)thiazol-4-yl]acetate

Referential Example 12

2-[2-(3-Fluoroanilino)thiazol-4-yl]acetic acid hydrochloride

[0042]

Referential Example 13

To a solution of 0.96 g of ethyl 3-oxovalerate in 4 ml of acetic acid was added 2.1 g of pyridinium tribromide. The mixture was stirred at room temperature for three hour, then diethyl ether and water were added thereto, and the organic layer was washed with water and a saturated saline solution. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated therefrom to give 1.24 g of a crude bromine compound. To a solution of 1.24 g of the crude bromine compound in ethanol was added 0.5 g of thiourea. After heating to reflux for 12 hours, the solvent was concentrated, and the concentrate was recrystallized from ethanol-ethyl acetate to give 1.05 g of ethyl 2-(2-amino-5-methylthiazol-4-yl)acetate.

[0043]

The compound of Referential Example 14 was prepared by the same manner as in Referential Example 4.

Referential Example 14

2-(2-Amino-5-methylthiazol-4-yl)acetic acid hydrochloride

Referential Example 15

To a solution of 0.8 g of methyl 2-(5-sulfanyl-1H-1,2,4-triazol-3-yl)acetate in 16 ml of acetonitrile were added 0.79 g of benzyl bromide and 1.5 g of cesium carbonate. The mixture was stirred at room temperature for 30 minutes, insoluble matters were filtered off, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel

column chromatography (eluent: chloroform/methanol = 50/1) to give 0.79 g of ethyl 2-(5-benzylsulfanyl-1H-1,2,4-triazol-3-yl)acetate.

[0044]

The compounds of Referential Examples 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47 and 49 were prepared by the same manner as in Referential Example 2; and the compounds of Referential Examples 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48 and 50 were prepared by the same manner as in Referential Example 4.

Referential Example 16

2-(5-Benzylsulfanyl-1H-1,2,4-triazol-3-yl)acetic acid hydrochloride

Referential Example 17

Ethyl 2-[1-(4-fluorobenzyl)-1H-imidazol-2-yl]acetate

Referential Example 18

2-[1-(4-Fluorobenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 19

Ethyl 2-[1-(4-chlorobenzyl)-1H-imidazol-2-yl]acetate

Referential Example 20

2-[1-(4-Chlorobenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

[0045]

Referential Example 21

Ethyl 2-[1-(3-chlorobenzyl)-1H-imidazol-2-yl]acetate

Referential Example 22

2-[1-(3-Chlorobenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 23

Ethyl 2-[1-(2-chlorobenzyl)-1H-imidazol-2-yl]acetate

Referential Example 24

2-[1-(2-Chlorobenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 25

Ethyl 2-[1-(3,4-dichlorobenzyl)-1H-imidazol-2-yl]-acetate

Referential Example 26

2-[1-(3,4-Dichlorobenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 27

Ethyl 2-[1-(4-bromobenzyl)-1H-imidazol-2-yl]acetate

Referential Example 28

2-[1-(4-Bromobenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 29

Ethyl 2-[1-(4-iodobenzyl)-1H-imidazol-2-yl]acetate

Referential Example 30

2-[1-(4-Iodobenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

[0046]

Referential Example 31

Ethyl 2-[1-(4-trifluoromethylbenzyl)-1H-imidazol-2-yl]acetate

Referential Example 32

2-[1-(4-Trifuoromethylbenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 33

Ethyl 2-[1-(4-isopropylbenzyl)-1H-imidazol-2-yl]-acetate

Referential Example 34

2-[1-(4-Isopropylbenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 35

Ethyl 2-[1-(4-phenylbenzyl)-1H-imidazol-2-yl]acetate

Referential Example 36

2-[1-(4-Phenylbenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 37

Ethyl 2-[1-(2-naphthyl)-1H-imidazol-2-yl]acetate

Referential Example 38

2-[1-(2-Naphthyl)-1H-imidazol-2-yl]acetic acid hydro-chloride

Referential Example 39

Ethyl 2-[1-(2-pyridyl)methyl-1H-imidazol-2-yl]acetate

Referential Example 40

2-[1-(2-Pyridyl)methyl-1H-imidazol-2-yl]acetic acid hydrochloride

[0047]

Referential Example 41

Ethyl 2-[1-(2-methyl-2-propenyl)-1H-imidazol-2-yl]-acetate

Referential Example 42

2-[1-(2-Methyl-2-propenyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 43

Ethyl 2-[1-benzyl-1H-imidazol-4-yl]acetate

Referential Example 44

2-(1-Benzyl-1H-imidazol-4-yl)acetic acid hydrochloride

Referential Example 45

Ethyl 2-[1-(2-chlorobenzyl)-1H-imidazol-4-yl]acetate

Referential Example 46

2-[1-(2-Chlorobenzyl)-1H-imidazol-4-yl]acetic acid hydrochloride

Referential Example 47

Ethyl 2-[1-(3-chlorobenzyl)-1H-imidazol-4-yl]acetate

Referential Example 48

2-[1-(3-chlorobenzyl)-1H-imidazol-4-yl]acetic acid hydrochloride

Referential Example 49

Ethyl 2-[1-(4-chlorobenzyl)-1H-imidazol-4-yl]acetate

Referential Example 50

2-[1-(4-Chlorobenzyl)-1H-imidazol-4-yl]acetic acid hydrochloride

[0048]

Referential Example 51

To a solution of 0.66 g of ethyl 2-(1H-1,2,4-triazol-3-yl)acetate in 10 ml of acetonitrile were added 0.59 g of potassium carbonate and 0.73 g of benzyl bromide. The mixture was heated to reflux for two hours, insoluble matters were filtered off, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 3/2) to give 289 mg of ethyl 2-(2-benzyl-1H-1,2,4-triazol-3-yl)acetate (Referential Example 51a) and 311 mg of ethyl 2-(1-benzyl-1H-1,2,4-triazol-3-yl)acetate (Referential Example 51b).

[0049]

The compounds of Referential Examples 52 and 53 were prepared by the same manner as in Referential Example 4.

Referential Example 52

2-(2-Benzyl-1H-1,2,4-triazol-3-yl)acetic acid hydrochloride

Referential Example 53

2-(1-Benzyl-1H-1,2,4-triazol-3-yl)acetic acid hydrochloride

[0050]

The compounds of Referential Examples 54(a) and 54(b) were prepared by the same manner as in Referential Example 51.

Referential Example 54(a)

Ethyl 2-[1-(4-fluorobenzyl)-1H-tetrazol-5-yl]acetate

Referential Example 54(b)

Ethyl 2-[2-(4-fluorobenzyl)-1H-tetrazol-5-yl]acetate

[0051]

The compounds of Referential Examples 55 and 56 were prepared by the same manner as in Referential Example 5.

Referential Example 55

2-[1-(4-Fluorobenzyl)-1H-tetrazol-5-yl]acetic acid

Referential Example 56

2-[2-(4-Fluorobenzyl)-1H-tetrazol-5-yl]acetic acid

[0052]

The compounds of Referential Examples 57(a) and 57(b) were prepared by the same manner as in Referential Example 51.

Referential Example 57(a)

Ethyl 2-[1-(3,4-dichlorobenzyl)-1H-tetrazol-5-yl]-acetate

Referential Example 57(b)

Ethyl 2-[2-(3,4-dichlorobenzyl)-1H-tetrazol-5-yl]-acetate

[0053]

The compounds of Referential Examples 58 and 59 were prepared by the same manner as in Referential Example 5.

Referential Example 58

2-[1-(3,4-Dichlorobenzyl)-1H-tetrazol-5-yl]acetic acid

Referential Example 59

2-[2-(3,4-Dichlorobenzyl)-1H-tetrazol-5-yl]acetic acid

[0054]

Referential Example 60

Into a mixture of 3.67 g of 1-phenyl-2-methyl-1H-imidazole with 50 ml of acetonitrile and 6.50 ml of triethylamine was dropped 4.40 ml of ethyl chloroformate with ice cooling and stirring in an argon atmosphere. After 2.5 hours, water and ethyl acetate were added to the reaction mixture, and the organic layer was washed with a saturated saline solution and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 50/1) to give 2.26 g of ethyl 2-(1-phenyl-1H-imidazol-2-yl)acetate.

[0055]

The compounds of Referential Examples 61, 63 and 65 were prepared by the same manner as in Referential Example 4; and the compounds of Referential Examples 60 and 64 were prepared by the same manner as in Referential Example 60.

Referential Example 61

2-(1-Phenyl-1H-imidazol-2-yl)acetic acid hydrochloride

Referential Example 62

Ethyl 2-[1-(4-nitrobenzyl)-1H-imidazol-2-yl]acetate

Referential Example 63

2-[1-(4-Nitrobenzyl)-1H-imidazol-2-yl]acetic acid hydrochloride

Referential Example 64

Ethyl 2-[1-(2-phenylethyl)-1H-imidazol-2-yl]acetate

Referential Example 65

2-[1-(2-Phenylethyl)-1H-imidazol-2-yl]acetic acid hydrochloride

[0056]

Referential Example 66

Into a mixture of 3.69 g of 2,4-dimethyl-1H-imidazole, 4.27 g of triethylamine and 25 ml of acetonitrile was dropped 3.00 g of acetyl chloride with ice cooling and stirring. The reaction mixture was stirred at room temperature for 15 minutes, insoluble matters were filtered off, and the solvent was evaporated *in vacuo*. To the residue were added 7.11 g of 4-fluorobenzyl bromide and 30 ml of acetonitrile, and the mixture was heated to reflux for 3.5 hours. The solvent was evaporated *in vacuo*, ethanol and ethyl acetate were added to the residue, and the deposited crystals were collected by filtration and washed with ethyl acetate. To the resulting

crystals were added 100 ml of chloroform and 40 ml of a 0.5N aqueous solution of sodium hydroxide, and the organic layer was washed with a saturated saline solution and dried over anhydrous magnesium sulfate. The solvent was evaporated *in vacuo* to give 3.40 g of 1-(4-fluorobenzyl)-2,5-dimethyl-1H-imidazole.

[0057]

The compounds of Referential Examples 67 and 68 were prepared by the same manner as in Referential Examples 60 and 4, respectively.

Referential Example 67

Ethyl 2-[1-(4-fluorobenzyl)-5-methyl-1H-imidazol-2-yl]acetate

Referential Example 68

2-[1-(4-Fluorobenzyl)-5-methyl-1H-imidazol-2-yl]-acetic acid hydrochloride

[0058]

Referential Example 69

To a solution of 1.00 g of 2,4-dimethyl-1H-imidazole in 10 ml of dimethyl formamide was added 1.30 g of potassium tert-butoxide with stirring at room temperature. Into the mixture was dropped 2.20 g of 4-fluorobenzyl bromide, followed by stirring for one hour. After insoluble matters were filtered off, the solvent was evaporated *in vacuo*, and ethyl acetate and water were added to the residue. The organic layer was washed with a saturated saline solution and dried over anhydrous

magnesium sulfate. The solvent was evaporated *in vacuo*, and the residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 50/1) to give 1.17 g of 1-(4-fluorobenzyl)-2,4-dimethyl-1H-imidazole.

[0059]

The compounds of Referential Examples 70 and 71 were prepared by the same manner as in Referential Examples 60 and 4, respectively.

Referential Example 70

Ethyl 2-[1-(4-fluorobenzyl)-4-methyl-1H-imidazol-2-yl]acetate

Referential Example 71

2-[1-(4-Fluorobenzyl)-4-methyl-1H-imidazol-2-yl]-acetic acid hydrochloride

[0060]

Referential Example 72

Into a solution of 3.11 g of 2-benzyloxy-6-methylpyridine in 50 ml of tetrahydrofuran was dropped 16 ml of 1.03M sec-butyl lithium/cyclohexane at -78°C. Then, 0.95 ml of diethyl carbonate was added thereto at -78°C, the dry ice-methanol bath was removed, and the reaction solution was stirred until it rose to room temperature. The solvent was evaporated, and the residue was diluted with water and extracted with ethyl acetate. The resulting organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The resulting residue

was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 10/1) to give ethyl 2-(2-benzyloxypyridin-6-yl)acetate.

[0061]

The compounds of Referential Examples 73 and 75 were prepared by the same manner as in Referential Example 5; and the compound of Referential Example 74 was prepared by the same manner as in Referential Example 72.

Referential Example 73

2-(2-Benzyloxypyridin-6-yl)acetic acid

Referential Example 74

Ethyl 2-(2-tert-butoxycarbonylaminopyridin-6-yl)-acetate

Referential Example 75

2-(2-tert-Butoxycarbonylaminopyridin-6-yl)acetic acid

[0062]

Referential Example 76

Into a solution of 3.11 g of 5,6,7,8-tetrahydroquinoline in 15 ml of tetrahydrofuran was dropped 15 ml of 1.59M n-butyl lithium/hexane at not higher than -65°C. Then, 1.4 ml of diethyl carbonate was added thereto at -70°C, the dry ice-methanol bath was removed, and the reaction solution was stirred until it rose to room temperature. To the reaction solution were added water and ethyl acetate successively. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was

evaporated therefrom. The resulting residue was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 2/1) to give 3.0 g of a mixture of ethyl 8-(5,6,7,8-tetrahydro-quinoline)carboxylate and 5,6,7,8-tetrahydro-quinoline. To an ethanolic solution of 1.02 g of this mixture was added 5 ml of a 1N aqueous sodium hydroxide solution at room temperature. The reaction solution was stirred at room temperature for 12 hours, and the reaction solution was washed with diethyl ether twice to remove the 5,6,7,8-tetrahydro-quinoline. The reaction mixture was neutralized by adding 1N hydrochloric acid thereto, and the solvent was evaporated to give 750 mg of 8-(5,6,7,8-tetrahydroquinoline)carboxylic acid.

[0063]

Referential Example 77

To a mixed solution of ethyl acetate and a 1N aqueous solution of sodium hydroxide was added 25.2 g of 4-nitrophenyl ethylamine hydrochloride, and the mixture was vigorously stirred. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. To the resulting residue were added 100 ml of 2-propanol and 15.0 g of (R)-styrene oxide successively, and the reaction mixture was heated to reflux for 12 hours. The solvent was evaporated *in vacuo*, and the residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 100/1 → 10/1). The resulting residue was again subjected to silica gel column chromatography

(eluent: hexane/ethyl acetate/triethylamine = 1/5/trace) to give 8.05 g of (R)-1-phenyl-2-[[2-(4-nitrophenyl)ethyl]-amino]ethanol.

[0064]

Referential Example 78

A solution of 6.30 g of (R)-1-phenyl-2-[[2-(4-nitrophenyl)ethyl]amino]ethanol and 6.30 g of di-tert-butyl dicarbonate in 80 ml of tetrahydrofuran was stirred for 12 hours at room temperature. The residue obtained by evaporation of the solvent was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 3/1) to give 10.8 g of tert-butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-(4-nitrophenyl)ethyl]-carbamate.

[0065]

Referential Example 79

To a solution of tert-butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-(4-nitrophenyl)ethyl]carbamate in 200 ml of ethanol was added 1.03 g of 10% palladium-carbon and the mixture was stirred for two hours at room temperature in a hydrogen atmosphere under atmospheric pressure. Insoluble matters were removed using Celite, and the filtrate was concentrated *in vacuo* to give 9.54 g of tert-butyl (R)-N-[2-(4-aminophenyl)-N-(2-hydroxy-2-phenylethyl)ethyl]carbamate.

[0066]

Referential Example 80

To a solution of 7.62 g of (R)-mandelic acid in 100 ml of dimethylformamide were added 10.15 g of 4-nitrophenethylamine hydrochloride, 7.11 g of 1-hydroxybenzotriazole, 7.3 ml of triethylamine and 1.01 g of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and the reaction mixture was stirred at room temperature for 18 hours. To the mixture were added water and ethyl acetate, and the organic layer was washed with 1N hydrochloric acid, a saturated aqueous solution of sodium hydrogen carbonate, water and a saturated saline solution successively and dried over anhydrous magnesium sulfate. The solvent was evaporated to give 14.94 g of (R)-2-hydroxy-N-[(2-(4-nitrophenyl)ethyl]-2-phenylacetamide.

[0067]

Referential Example 81

To a solution of 14.94 g of (R)-2-hydroxy-N-[(2-(4-nitrophenyl)ethyl]-2-phenylacetamide in 80 ml of tetrahydrofuran was added 15.4 ml of a 10M borane-methyl sulfide complex, and the mixture was heated to reflux for 1.5 hours. This was cooled down to room temperature, stirred for one hour after addition of 20 ml of methanol, then 150 ml of 1N hydrochloride acid was added, and the mixture was heated to reflux for one hour. To the residue obtained by concentrating the solvent *in vacuo* were added 200 ml of 1N sodium hydroxide

and ethyl acetate, and the organic layer was washed with water and a saturated saline solution successively and dried over anhydrous magnesium sulfate. The solvent was evaporated *in vacuo*, the residue was dissolved in 100 ml of ethanol, and 12.3 ml of a 4N hydrogen chloride-ethyl acetate solution was added thereto. The deposited crystals were filtered to give 12.13 g of (R)-2-[2-(4-nitrophenyl)ethylamine]-1-phenylethanol hydrochloride.

[0068]

Referential Example 82

To a solution of 448 mg of tert-butyl (R)-N-[2-(4-aminophenyl)-N-(2-hydroxy-2-phenylethyl)ethyl]carbamate and 330 mg of triethylamine in 4 ml of chloroform was added 146 mg of 2-pyridinecarbonyl chloride. The reaction solution was stirred at room temperature for two hours, and the solvent was evaporated *in vacuo*. The residue was diluted with chloroform, and the organic layer was washed with a saturated aqueous solution of sodium hydrogen carbonate and dried over anhydrous magnesium sulfate. The residue obtained by evaporating the solvent *in vacuo* was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 1/3) to give 321 mg of tert-butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[(2-pyridinecarbonyl)amino]phenyl]ethyl]carbamate.

[0069]

The compound of Referential Example 83 was prepared by the same manner as in Referential Example 82.

Referential Example 83

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[(3-pyridinecarbonyl)amino]phenyl]ethyl]carbamate

Referential Example 84

To a solution of 377 mg of tert-butyl (R)-N-[2-(4-aminophenyl)-N-(2-hydroxy-2-phenylethyl)ethyl]carbamate in 10 ml of tetrahydrofuran were added 203 mg of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 143 mg of 1-hydroxybenzotriazole and 202 mg of 8-quinolinecarboxylic acid successively. The reaction solution was stirred at room temperature for 18.5 hours, and the solvent was evaporated *in vacuo*. The residue was diluted with ethyl acetate, and the organic layer was washed with a saturated aqueous solution of sodium hydrogen carbonate and dried over anhydrous magnesium sulfate. The residue obtained by evaporation of the solvent was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 2/1) to give 302 mg of tert-butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[(8-quinoline-carbonyl)amino]phenyl]ethyl]carbamate.

[0070]

The compounds of Referential Examples 85 to 139 were prepared by the same manner as in Referential Example 84.

Referential Example 85

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-(E)-N-[2-[4-[3-(2-pyridyl)acryloylamino]phenyl]ethyl]carbamate

Referential Example 86

tert-Butyl (R)-N-[2-[4-[(2-benzothiazol-2-ylacetyl)-amino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 87

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[[2-(imidazo[2,1-b]thiazol-3-yl)acetyl]amino]phenyl]ethyl]-carbamate

Referential Example 88

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-(2-methylthiazol-4-yl)acetylamino]phenyl]ethyl]carbamate

Referential Example 89

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-(1H-imidazol-2-yl)acetamino]phenyl]ethyl]carbamate

Referential Example 90

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[(2-1H-tetrazol-5-yl)acetamino]phenyl]ethyl]carbamate

Referential Example 91

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-(5-sulfanyl-1H-1,2,4-triazol-3-yl)acetylamino]phenyl]-ethyl]carbamate

Referential Example 92

tert-Butyl (R)-N-[2-[4-[[2-(2-aminothiazol-4-yl)-2-oxoacetyl]amino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 93

tert-Butyl (R)-N-[2-[4-[2-(5-amino-1,2,4-thiadiazol-3-yl)acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 94

tert-Butyl (R)-N-[2-[4-[2-(5-ethoxycarbonylamino-1,2,4-thiadiazol-3-yl)acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 95

tert-Butyl (R)-N-[2-[4-[2-[(3-fluorophenylamino)-thiazol-4-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 96

tert-Butyl (R)-N-[2-[4-[2-[(2-chloropyridin-6-yl)-acetyl]amino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 97

tert-Butyl (R)-N-[2-[4-[[2-(2-benzyloxypyridin-6-yl)-acetyl]amino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 98

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(2-methyl-3-propenyl)-1H-imidazol-2-yl)acetamino]-phenyl]ethyl]carbamate

Referential Example 99

tert-Butyl (R)-N-[2-[4-[2-(1-benzyl-1H-imidazol-4-yl)acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 100

tert-Butyl (R)-N-[2-[4-[2-[1-(2-chlorobenzyl)-1H-imidazol-4-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

[0071]

Referential Example 101

tert-Butyl (R)-N-[2-[4-[2-[1-(3-chlorobenzyl)-1H-imidazol-4-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 102

tert-Butyl (R)-N-[2-[4-[2-[1-(4-chlorobenzyl)-1H-imidazol-4-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 103

tert-Butyl (R)-N-[2-[4-[2-[1-(4-fluorobenzyl)-1H-imidazol-2-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 104

tert-Butyl (R)-N-[2-[4-[2-[1-(4-chlorobenzyl)-1H-imidazol-2-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 105

tert-Butyl (R)-N-[2-[4-[2-[1-(4-bromobenzyl)-1H-imidazol-2-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 106

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(4-iodobenzyl)-1H-imidazol-2-yl]acetamino]phenyl]-ethyl]carbamate

Referential Example 107

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(4-trifluoromethylbenzyl)-1H-imidazol-2-yl]-acetamino]phenyl]ethyl]carbamate

Referential Example 108

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(2-naphthyl)-1H-imidazol-2-yl]acetamino]phenyl]-ethyl]carbamate

Referential Example 109

tert-Butyl (R)-N-[2-[4-[2-[3-(4-fluorobenzyl)-4-methyl-1H-imidazol-2-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 110

tert-Butyl (R)-N-[2-[4-[2-[1-(4-fluorobenzyl)-4-methyl-1H-imidazol-2-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

[0072]

Referential Example 111

tert-Butyl (R)-N-[2-[4-[2-[1-(4-fluoromobenzyl)-1H-tetrazol-5-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 112

tert-Butyl (R)-N-[2-[4-[2-[2-(3,4-dichlorobenzyl)-1H-tetrazol-5-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 113

tert-Butyl (R)-N-[2-[4-[2-[2-(4-fluorobenzyl)-1H-tetrazol-5-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 114

tert-Butyl (R)-N-[2-[4-[2-[2-(3,4-dichlorobenzyl)-1H-tetrazol-5-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 115

tert-Butyl (R)-N-[2-[4-[2-(1H-1,2,4-triazol-3-yl]-acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 116

tert-Butyl (R)-N-[2-[4-[2-(5-benzylsulfanyl-1H-1,2,4-triazol-3-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 117

tert-Butyl (R)-N-[2-[4-[2-(2-acetamidothiazol-4-yl)-acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 118

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-(2-methanesulfonamidothiazol-4-yl]acetylamino]phenyl]-ethyl]carbamate

Referential Example 119

tert-Butyl (R)-N-[2-[4-[2-(2-guanidinothiazol-4-yl)-acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 120

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(2-phenylaminothiazol-4-yl)]acetamino]phenyl]ethyl]-carbamate

[0073]

Referential Example 121

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(4-nitrobenzyl)-1H-imidazol-2-yl]acetamino]phenyl]-ethyl]carbamate

Referential Example 122

tert-Butyl (R)-N-[2-[4-[2-(2-aminothiazol-4-yl)-acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 123

tert-Butyl (R)-N-[2-[4-[(2-aminothiazol-4-yl)-carboxyamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 124

tert-Butyl (R)-N-[2-[4-[2-(2-amino-5-methylthiazol-4-yl)acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 125

tert-Butyl (R)-N-[2-[4-[2,2-dimethyl-2-(2-amino-thiazol-4-yl)acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 126

tert-Butyl (R)-N-[2-[4-[(2-amino-4,5,6,7-tetrahydro-benzothiazol-4-yl)carboxyamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 127

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[[2-(imidazo[2,1-b]thiazol-6-yl)acetyl]amino]phenyl]ethyl]-carbamate

Referential Example 128

tert-Butyl (R)-N-[2-[4-[2-(2-benzyl-1,2,4-triazol-3-yl)acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 129

tert-Butyl (R)-N-[2-[4-[2-(1-benzyl-1,2,4-triazol-3-yl)acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 130

tert-Butyl (R)-N-[2-[4-[2-(3-benzyl-2-thioxothiazol-4-yl)acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

[0074]

Referential Example 131

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[[(5,6,7,8-tetrahydroquinolin-8-yl)carbonyl]amino]phenyl]-ethyl]carbamate

Referential Example 132

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[(1-phenyl)-1H-imidazol-2-yl]acetamino]phenyl]ethyl]-carbamate

Referential Example 133

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(4-isopropylbenzyl)-1H-imidazol-2-yl]acetamino]-phenyl]ethyl]carbamate

Referential Example 134

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(4-phenylbenzyl)-1H-imidazol-2-yl]acetamino]phenyl]-ethyl]carbamate

Referential Example 135

tert-Butyl (R)-N-[2-[4-[2-[1-(2-chlorobenzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 136

tert-Butyl (R)-N-[2-[4-[2-[1-(3-chlorobenzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 137

tert-Butyl (R)-N-[2-[4-[2-[1-(3,4-dichlorobenzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 138

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(2-pyridyl)methyl-1H-imidazol-2-yl]acetylamino]-phenyl]ethyl]carbamate

Referential Example 139

tert-Butyl (R)-N-[2-[4-[[2-[2-(tert-butoxycarbonyl-amino)pyridin-6-yl]acetyl]amino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

[0075]

Referential Example 140

To a solution of 1.1 g of tert-butyl (R)-N-[2-[4-[[2-[2-(tert-butoxycarbonylamino)pyridin-6-yl]acetylamino]-phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate in 10 ml of methanol was added 20 ml of a 4N hydrogen chloride-ethyl acetate solution. The reaction solution was stirred at room temperature for two hours. The solvent was evaporated, and to the resulting residue were added 5.2 g of triethylamine, 2.2 g of di-tert-butyl carbonate, 15 ml of tetrahydrofuran and 1 ml of methanol, and the mixture was stirred for 13 hours. The reaction mixture was diluted with ethyl acetate and washed with a saturated aqueous solution of sodium chloride and a saturated aqueous solution of sodium hydrogen carbonate successively. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated *in vacuo*. The resulting residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 100/1) to give 260 mg of tert-butyl (R)-N-[2-[4-[[2-(2-aminopyridin-6-yl)acetyl]amino]phenyl]-ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate.

[0076]

Referential Example 141

tert-butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(2-methyl-2-propenyl)-1H-imidazol-2-yl]acetamino]-phenyl]ethyl]carbamate (314 mg) was dissolved in 15 ml of ethanol, 90 mg of 10% palladium-carbon was added, and the mixture

was stirred for 5.5 hours in a nitrogen atmosphere under atmospheric pressure. The catalyst was filtered off, the solvent was evaporated *in vacuo*, and the residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 30/1) to give 230 mg of tert-butyl (R)-N-[(2-hydroxy-2-phenyl)ethyl]-N-[2-[4-[1-(2-methyl-propyl)-1H-imidazol-2-yl]acetamino]phenyl]ethyl]carbamate.

[0077]

Referential Example 142

To a solution of 403 mg of tert-butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[(2-1H-imidazol-2-ylacetyl)-amino]phenyl]ethyl]carbamate in 10 ml of acetonitrile were added 120 mg of potassium carbonate and 164 mg of 2-fluorobenzyl bromide successively at room temperature. The reaction solution was stirred at 50°C for 12 hours. Insoluble matters were filtered off using Celite, and the solvent was evaporated. The resulting residue was purified by silica gel column chromatography to give 253 mg of tert-butyl (R)-N-[2-[4-[[2-[1-(2-fluorobenzyl)-1H-imidazol-2-yl]acetyl]amino]-phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate.

[0078]

The compounds of Referential Examples 143 to 162 were prepared by the same manner as in Referential Example 142.

Referential Example 143

tert-Butyl (R)-N-[2-[4-[2-[1-(3-fluorobenzyl)-1H-imidazol-2-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 144

tert-Butyl (R)-N-[2-[4-[2-[1-(2,4-difluorobenzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 145

tert-Butyl (R)-N-[2-[4-[2-[1-(2,6-difluorobenzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 146

tert-Butyl (R)-N-[2-[4-[[2-[1-(3,5-difluorobenzyl)-1H-imidazol-2-yl]acetyl]amino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 147

tert-Butyl (R)-N-[2-[4-[2-[1-(2,5-difluorobenzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 148

tert-Butyl (R)-N-[2-[4-[2-[1-(3,4-difluorobenzyl)-1H-imidazol-2-yl]acetamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 149

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(2,3,5-trifluorobenzyl)-1H-imidazol-2-yl]acetamino]-phenyl]ethyl]carbamate

Referential Example 150

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[[2-[1-(2,4,5-trifluorobenzyl)-1H-imidazol-2-yl]acetyl]-amino]phenyl]ethyl]carbamate

Referential Example 151

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(3,4,5-trifluorobenzyl)-1H-imidazol-2-yl]acetamino]-phenyl]ethyl]carbamate

[0079]

Referential Example 152

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[[2-[1-(2,3,4,5,6-pentafluorobenzyl)-1H-imidazol-2-yl]-acetylamino]phenyl]ethyl]carbamate

Referential Example 153

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[[2-[1-(3-iodobenzyl)-1H-imidazol-2-yl]acetyl]amino]phen-yl]ethyl]carbamate

Referential Example 154

tert-Butyl (R)-N-[2-[4-[2-[1-(2,6-dichlorobenzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 155

tert-Butyl (R)-N-[2-[4-[2-[1-(4-cyanobenzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 156

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(quinolin-2-yl)methyl-1H-imidazol-2-yl]acetylamino]-phenyl]ethyl]carbamate

Referential Example 157

tert-Butyl (R)-N-[2-[4-[2-[1-(2-chloro-6-fluoro-benzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 158

tert-Butyl (R)-N-[2-[4-[2-[1-(2-chloro-4-fluoro-benzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 159

tert-Butyl (R)-N-[2-[4-[2-[1-(2,5-dichlorobenzyl)-1H-imidazol-2-yl]acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate

Referential Example 160

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-(2,3,4-trifluorobenzyl)-1H-imidazol-2-yl]acetyl-amino]phenyl]ethyl]carbamate

Referential Example 161

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[[2-[1-(4-methoxycarbonylbenzyl)-1H-imidazol-2-yl]acetyl]-amino]phenyl]ethyl]carbamate

Referential Example 162

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-[1-[4-(piperidin-1-carnbonyl)benzyl]-1H-imidazol-2-yl]-acetylamino]phenyl]ethyl]carbamate

[0080]

Referential Example 163

Into a solution of 1.87 g of tert-butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-(4-nitrophenyl)ethyl]carbamate and 1.05 g of diisopropyl ethylamine in 40 ml of chloroform was dropped a solution of 1.07 g of bromoacetyl bromide in 3 ml of chloroform with ice cooling. The reaction mixture was stirred for one hour with ice cooling and washed with 1N hydrochloric acid and a saturated saline solution successively. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated *in vacuo*. The resulting residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 30:1) to give 2.15 g of tert-butyl (R)-N-[2-[4-(2-bromoacetylamino)phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate.

[0081]

The compounds of Referential Examples 164 to 166 were prepared by the same manner as in Referential Example 147, and the compound of Referential Example 167 was prepared by the same manner as in Referential Example 77.

Referential Example 164

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-(1-pyrazolyl)acetylamino]phenyl]ethyl]carbamate

Referential Example 165

tert-Butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[2-(1,2,4-triazol-1-yl)acetylamino]phenyl]ethyl]carbamate

Referential Example 166

tert-Butyl (R)-N-[2-[4-[2-(2-aminobenzimidazol-1-yl)-acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)-carbamate

Referential Example 167

(R)-2-[N-Benzyl-N-[2-(4-nitrophenyl)ethyl]amino]-1-phenylethanol

[0082]

Referential Example 168

To a solution of (R)-2-[N-benzyl-N-[2-(4-nitro-phenyl)ethyl]amino]-1-phenylethanol in 150 ml of methanol were added 8.6 g of iron powder and 40 ml of 2N hydrochloric acid. The reaction mixture was heated to reflux for two hours, 1N sodium hydroxide was added thereto, and the insoluble matters thus produced were filtered off using Celite. The filtrate was

concentrated *in vacuo* to remove the methanol. The resulting aqueous phase was extracted with chloroform, the organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated *in vacuo*. The resulting residue was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 1/1) to give 11.45 g of (R)-2-[N-[2-(4-aminophenyl)-ethyl]-N-benzylamino]-1-phenylethanol.

[0083]

The compounds of Referential Examples 169 to 174 were prepared by the same manner as in Referential Example 84.

Referential Example 169

(R)-4'-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]-2-(2-pyridyl)acetanilide

Referential Example 170

(R)-4'-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]-2-(3-pyridyl)acetanilide

Referential Example 171

(R)-4'-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]-2-(4-pyridyl)acetanilide

Referential Example 172

(R)-4'-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]-(E)-3-(2-pyridyl)acrylic anilide

Referential Example 173

(R)-4'-[4-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]phenyl]-2-[1-(2-phenylethyl)-1H-imidazol-2-yl]acetanilide

Referential Example 174

(R)-4'-[4-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]phenyl]-2-(1H-benzimidazol-2-yl]acetanilide

[0084]

Referential Example 175

To 502 mg of (R)-2-[N-[2-(4-aminophenyl)ethyl]-N-benzylamino]-1-phenylethanol were added 336 g of ethyl 2-(3-methylpyridin-2-yl)acetate and 10 ml of xylene. The reaction mixture was refluxed for nine hours, and the solvent was evaporated *in vacuo*. The resulting residue was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 1/3) to give 222 mg of (R)-4'-[2-[N-benzyl-N-(2-hydroxy-2-phenylethyl)amino]ethyl]-2-(3-methylpyridin-2-yl)-acetanilide.

[0085]

The compounds of Referential Examples 176 to 180 were prepared by the same manner as Referential Example 175.

Referential Example 176

(R)-4'-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl-2-(2-pyrazinyl)acetanilide

Referential Example 177

(R)-4'-[4-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]phenyl]-2-(1-benzyl-1H-imidazol-2-yl)acetanilide

Referential Example 178

(R)-4'-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]-2-(4-methyl-2-pyridyl)acetanilide

Referential Example 179

(R)-4'-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl-2-(5-methyl-2-pyridyl)acetanilide

Referential Example 180

(R)-4'-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl-2-(6-methyl-2-pyridyl)acetanilide

[0086]

Referential Example 181

To 5.22 g of 4-nitrophenylacetone were added 3.43 g of benzylamine and 50 ml of toluene. The reaction solution was heated to reflux for two hours while dehydration using a Dean-Starke apparatus. The solvent was evaporated *in vacuo*, the residue was dissolved in 100 ml of methanol and 30 ml of tetrahydrofuran, and 1.52 g of sodium borohydride was added to this solution at room temperature. The reaction solution was stirred for two hours at the same temperature, the solvent was evaporated *in vacuo*, and ethyl acetate and water were added to the residue. After separation of the liquid, the organic layer

was dried over anhydrous magnesium sulfate, and the solvent was evaporated *in vacuo*. The residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 100/1) to give 5.35 g of N-benzyl-N-[1-methyl-2-(4-nitrophenyl)-ethyl]amine.

[0087]

Referential Example 182

To 6.34 g of N-benzyl-N-[1-methyl-2-(4-nitrophenyl)-ethyl]amine was added (R)-styrene oxide. The reaction mixture was stirred for two hours at 150°C which was a temperature of the oil bath. The resulting mixture was purified by silica gel column chromatography (eluent: hexane/ethyl acetate = 10/1) to give 2.98 g of 2-[benzyl-N-[(R)-1-methyl-2-(4-nitrophenyl)ethyl]amino]-(R)-1-phenylethanol (Referential Example 182a) as a yellow oil and 2.69 g of 2-[benzyl-N-[(S)-1-methyl-2-(4-nitrophenyl)ethyl]amino]-(R)-1-phenylethanol (Referential Example 182b) as pale yellow crystals.

[0088]

The compounds of Referential Examples 183 and 184 were prepared by the same manner as in Referential Example 168; and the compounds of Referential Example 185 to 187 were prepared by the same manner in Referential Example 175.

Referential Example 183

2-[N-[2-(4-Aminophenyl)-(R)-1-methylethyl]-N-benzyl-amino]-(R)-1-phenylethanol

Referential Example 184

2-[N-[2-(4-Aminophenyl)-(S)-1-methylethyl]-N-benzyl-amino]-(R)-1-phenylethanol

Referential Example 185

4'-[(R)-2-[N-Benzyl-N-((R)-2-hydroxy-2-phenylethyl)-amino]propyl]-2-(2-pyridyl)acetanilide

Referential Example 186

4'-[(S)-2-[N-Benzyl-N-((R)-2-hydroxy-2-phenylethyl)-amino]propyl]-2-(2-pyridyl)acetanilide

Referential Example 187

4'-[(S)-2-[N-Benzyl-N-((R)-2-hydroxy-2-phenylethyl)-amino]propyl]-2-(1-benzyl-1H-imidazol-2-yl)acetanilide

[0089]

Referential Example 188

To a solution of 0.96 g of 2-fluoroacetophenone in 20 ml of tetrahydrofuran was added 2.65 g of benzyltrimethylammonium tribromide. The reaction mixture was stirred at room temperature for 30 minutes, insoluble matters were filtered off, and the solvent was concentrated *in vacuo*. The resulting residue was dissolved in 40 ml of 2-butanone, then 1.81 g of N-benzyl-N-nitrophenethylamine and 0.92 g of diisopropyl ethylamine were added, and the reaction mixture was heated to reflux for one hour. The solvent was evaporated *in vacuo*, ethyl acetate was added thereto, and the mixture was washed with water and a saturated saline solution successively. The organic

layer was dried over anhydrous magnesium sulfate and evaporated *in vacuo*. The resulting residue was dissolved in 40 ml of methanol, 0.34 g of sodium borohydride was added thereto, and the reaction mixture was stirred at room temperature for one hour. The solvent was evaporated *in vacuo*, ethyl acetate was added, and the mixture was washed with water and a saturated saline solution successively. The organic layer was dried over anhydrous magnesium sulfate and evaporated *in vacuo*. The resulting residue was purified by silica gel column chromatography (eluent: chloroform) to give 1.95 g of 2-[N-benzyl-N-[2-(4-nitrophenyl)ethyl]amino]-1-(2-fluorophenyl)-ethanol.

[0090]

The compounds of Referential Examples 189 and 190 were prepared by the same manner as in Referential Example 188; the compounds of Referential Examples 191 to 193 were prepared by the same manner as in Referential Example 168; the compound of Referential Example 194 was prepared by the same manner as in Referential Example 84; and the compounds of Referential Examples 195 and 196 were prepared by the same manner as in Referential Example 175.

Referential Example 189

2-[N-Benzyl-N-[2-(4-nitrophenyl)ethyl]amino]-1-(3-fluorophenyl)ethanol

Referential Example 190

2-[N-Benzyl-N-[2-(4-nitrophenyl)ethyl]amino]-1-(4-fluorophenyl)ethanol

Referential Example 191

2-[N-[2-(4-Aminophenyl)ethyl]-N-benzylamino]-1-(2-fluorophenyl)ethanol

Referential Example 192

2-[N-[2-(4-Aminophenyl)ethyl]-N-benzylamino]-1-(3-fluorophenyl)ethanol

Referential Example 193

2-[N-[2-(4-Aminophenyl)ethyl]-N-benzylamino]-1-(4-fluorophenyl)ethanol

Referential Example 194

4'-[2-[N-Benzyl-N-[2-(2-fluorophenyl)-2-hydroxy-ethyl]amino]ethyl]-2-(2-pyridyl)acetanilide

Referential Example 195

4'-[2-[N-Benzyl-N-[2-(3-fluorophenyl)-2-hydroxy-ethyl]amino]ethyl]-2-(2-pyridyl)acetanilide

Referential Example 196

4'-[2-[N-Benzyl-N-[2-(4-fluorophenyl)-2-hydroxy-ethyl]amino]ethyl]-2-(2-pyridyl)acetanilide

[0091]

Referential Example 197

A reaction mixture of 5.12 g of methyl 2-pyridylacetate, 5.14 g of 4-aminobenzyl cyanide and 50 ml of xylene was heated

to reflux for 24 hours. An appropriate amount of the solvent was evaporated, diethyl ether was added to the residue, and the resulting crystals were taken by filtration to give 5.65 g of 4'-cyanomethyl-2-(2-pyridyl)acetanilide.

[0092]

The compounds 198 to 201 were prepared by the same manner as in Referential Example 197.

Referential Example 198

4'-Cyanomethyl-2-(2-pyrimidinyl)acetanilide

Referential Example 199

4'-Cyanomethyl-2-(2-quinolyl)acetanilide

Referential Example 200

4'-Cyanomethyl-2-(2,4-dimethylpyridin-6-yl)acetanilide

Referential Example 201

2-[1-(4-Chlorobenzyl)-1H-benzimidazol-2-yl]-4'-cyanomethylacetanilide

[0093]

Referential Example 202

To a solution of 640 mg of 4'-cyanomethyl-2-(4,6-dimethyl-2-pyridyl)acetanilide in 15 ml of tetrahydrofuran was added 15 ml of an ethanolic suspension of a Raney nickel, and concentrated aqueous ammonia was added to adjust the pH of the mixture to about 10. The mixture was stirred at room temperature for one hour in a hydrogen atmosphere under

atmospheric pressure. The reaction mixture was filtered using Celite, and the solvent was evaporated *in vacuo* to give 640 mg of 4'-(2-aminomethyl)-2-(4,6-dimethyl-2-pyridyl)acetanilide.

[0094]

Referential Example 203

To a solution of 630 mg of 4'-(2-aminomethyl)-2-(4,6-dimethyl-2-pyridyl)acetanilide in 20 ml of toluene was added 0.27 ml of benzaldehyde, and the mixture was heated to reflux for three hours using a Dean-Starke apparatus. The reaction mixture was filtered, and the solvent was evaporated *in vacuo*. A solution of the resulting residue in 30 ml of methanol was cooled at 0°C, 63 mg of sodium borohydride was added, and the mixture was stirred at 0°C for one hour. About one-half of the solvent of the reaction mixture was evaporated *in vacuo*, water and ethyl acetate were added to the residue, the organic layer was washed with a saturated saline solution twice and dried *in vacuo* and the solvent was evaporated *in vacuo*. To a solution of the resulting residue in 50 ml of isopropanol was added 0.26 ml of (R)-styrene oxide, and the mixture was heated to reflux for 12 hours. The solvent was evaporated *in vacuo*, and the resulting residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 100/3) to give 920 mg of (R)-4'-[2-[N-benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]-2-(4,6-dimethyl-2-pyridyl)acetanilide.

[0095]

The compounds of Referential Examples 204 to 206 were prepared by the same manner as in Referential Example 84.

Referential Example 204

tert-Butyl N-[3-[4-[[2-(2-pyridyl)acetyl]amino]phenyl]propyl]carbamate

Referential Example 205

tert-Butyl N-[2-[4-[[2-(2-pyridyl)acetyl]amino]phenoxy]ethyl]carbamate

Referential Example 206

tert-Butyl N-[1,1-dimethyl-2-[4-[[2-(2-pyridyl)acetyl]amino]phenylethyl]carbamate

[0096]

Referential Example 207

To a solution of 1.54 g of tert-Butyl N-[3-[4-[[2-(2-pyridyl)acetyl]amino]phenyl]propyl]carbamate in 10 ml of methanol was added 10 ml of a 4N hydrogen chloride-ethyl acetate solution. The reaction mixture was stirred for two hours at room temperature, and the solvent was evaporated *in vacuo*. The residue was dissolved in a mixture of chloroform and 1N sodium hydroxide. The organic layer was dried over anhydrous magnesium sulfate, the solvent was evaporated *in vacuo*, and the resulting residue was dried to give 610 mg of 4'-(3-aminopropyl)-2-(2-pyridyl)acetanilide.

[0097]

Referential Example 208

To a solution of 1.1 g of tert-butyl (R)-N-[2-(4-aminophenyl)ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate in 20 ml of 1,2-dichloroethane were added 0.35 g of triethylamine and 0.64 g of 4-nitrophenyl chloroformate. The reaction mixture was stirred at room temperature for one hour, and the solvent was evaporated *in vacuo*. The resulting residue was dissolved in 15 ml of dimethylformamide, and 0.31 g of 2-aminopyridine was added thereto. The reaction mixture was stirred at room temperature for four hours, and ethyl acetate and water were added thereto. The organic layer was washed with water, a saturated sodium hydrogen carbonate solution and a saturated saline solution successively and dried over anhydrous magnesium sulfate. The solvent was evaporated *in vacuo*, and the resulting residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 30/1) to give 0.19 g of tert-butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[3-(2-pyridyl)ureido]phenyl]ethyl]carbamate.

[0098]

Example 1

A 4N hydrogen chloride-ethyl acetate solution (10 ml) was added to 10 ml of an ethanolic solution of 458 mg of tert-butyl (R)-N-(2-hydroxy-2-phenylethyl)-N-[2-[4-[(2-pyridinecarbonyl)amino]phenyl]ethyl]carbamate. The reaction solution was stirred at room temperature for three hours, and the solvent

was then evaporated *in vacuo*. The obtained crude crystals were recrystallized from methanol-ethanol-ethyl acetate to give 289 mg of (R)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]-2-pyridinecarboxanilide dihydrochloride.

[0099]

The compounds of Examples 2 to 4 were prepared by the same manner as in Example 1.

Example 2

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-3-pyridinecarboxanilide dihydrochloride

Example 3

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-8-quinolinecarboxanilide dihydrochloride

Example 4

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-(E)-3-(2-pyridyl)acrylic anilide dihydrochloride

Example 5

(R)-2-(Benzothiazol-2-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)-amino]ethyl]acetanilide dihydrochloride

Example 6

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(imidazo[2,1-b]thiazol-3-yl)acetanilide dihydrochloride

Example 7

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(2-methylthiazol-4-yl)acetanilide hydrochloride

Example 8

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(1H-imidazol-2-yl)acetanilide dihydrochloride

Example 9

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(1H-tetrazol-5-yl)acetanilide hydrochloride

Example 10

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(5-sulfanyl-1H-1,2,4-triazol-3-yl)acetanilide hydrochloride

[0100]

Example 11

(R)-2-(2-Aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]-2-oxoacetanilide dihydrochloride

Example 12

(R)-2-(5-Amino-1,2,4-thiadiazol-3-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 13

(R)-2-(5-Ethoxycarbonylamino-1,2,4-thiadiaol-3-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 14

(R)-2-[(2-(3-Fluorophenylamino)thiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 15

(R)-2-(2-Chloropyridin-6-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 16

(R)-2-(2-Benzyloxypyridin-6-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 17

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(2-methyl-3-propenyl)-1H-imidazol-2-yl)acetanilide dihydrochloride

Example 18

(R)-2-(1-Benzyl-1H-imidazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 19

(R)-2-[1-(2-Chlorobenzyl)-1H-imidazol-4-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 20

(R)-2-[1-(3-Chlorobenzyl)-1H-imidazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

[0101]

Example 21

(R)-2-[1-(4-Chlorobenzyl)-1H-imidazol-4-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 22

(R)-2-[1-(4-Fluorobenzyl)-1H-imidazol-2-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 23

(R)-2-[1-(4-Chlorobenzyl)-1H-imidazol-2-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 24

(R)-2-[1-(4-Bromobenzyl)-1H-imidazol-2-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 25

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(4-iodobenzyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

Example 26

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(4-trifluoromethylbenzyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

Example 27

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(2-naphthyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

Example 28

(R)-2-[1-(4-Fluorobenzyl)-5-methyl-1H-imidazol-2-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 29

(R)-2-[1-(4-Fluorobenzyl)-4-methyl-1H-imidazol-2-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 30

(R)-2-[1-(4-Fluorobenzyl)-1H-tetrazol-5-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

[0102]

Example 31

(R)-2-[2-(3,4-Dichlorobenzyl)-1H-tetrazol-5-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 32

(R)-2-[2-(4-Fluorobenzyl)-1H-tetrazol-5-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 33

(R)-2-[1-(3,4-Dichlorobenzyl)-1H-tetrazol-5-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

[0103]

Example 34

To a solution of 75 mg of tert-butyl (R)-N-[2-[4-[2-(1H-1,2,4-triazol-3-yl)acetylamino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate in 5 ml of methanol was added 4 ml of a solution of 4N hydrogen chloride in ethyl acetate. The mixture was stirred at room temperature for three hours, the solvent was filtered off, and the resulting powder was washed with ethanol. The resulting powder was dried to give 125 mg

of (R)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]-2-(1H-1,2,4-triazol-3-yl)acetanilide dihydrochloride.

[0104]

The compounds of Examples 35 to 40 were prepared by the same manner as in Example 34.

Example 35

(R)-2-(5-Benzylsulfanyl-1H-1,2,4-triazol-3-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 36

(R)-2-(2-Acetamidothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 37

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(2-methanesulfonamidothiazol-4-yl)acetanilide hydrochloride

Example 38

(R)-2-(2-Guanidinothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 39

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(2-phenylaminothiazol-4-yl)acetanilide hydrochloride

Example 40

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(4-nitrobenzyl)-1H-imidazol-2-yl]acetanilide hydrochloride

[0105]

Example 41

To 690 mg of tert-butyl (R)-N-[2-[4-[2-(2-amino-thiazol-4-yl)acetamino]phenyl]ethyl]-N-[(2-hydroxy-2-phenyl)ethyl]carbamate were added 30 ml of methanol and 15 ml of a solution of 4N hydrogen chloride in ethyl acetate, and the mixture was stirred at room temperature for two hours. The solvent was evaporated *in vacuo*, and the residue was purified by a reverses phase column chromatography (eluent: water/methanol = 2/1) to give 310 mg of (R)-2-(2-aminothiazol-4-yl)-4'-[2-(2-hydroxy-2-phenylethyl)amino]-ethyl]acetanilide dihydrochloride.

[0106]

The compounds of Examples 42 to 57 were prepared by the same manner as in Example 41.

Example 42

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-(2-amino-thiazol-4-yl)carboxylic acid anilide hydrochloride

Example 43

(R)-2-(2-Amino-5-methylthiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 44

(R)-2-(2-Aminothiazol-4-yl)-2-methyl-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]propionanilide hydrochloride

Example 45

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-(2-amino-4,5,6,7-tetrahydrobenzothiazol-4-yl)carboxylic acid anilide dihydrochloride

Example 46

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(imidazo[2,1-b]thiazol-6-yl)acetanilide hydrochloride

Example 47

(R)-2-(2-Benzyl-1H-1,2,4-triazol-3-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 48

(R)-2-(1-Benzyl-1H-1,2,4-triazol-3-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 49

(R)-2-(3-Benzyl-2-thioxothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 50

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-(5,6,7,8-tetrahydroquinolin-8-yl)carboxylic acid dihydrochloride

[0107]

Example 51

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(1-phenyl-1H-imidazol-2-yl)acetanilide dihydrochloride

Example 52

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[(1-(4-isopropylbenzyl)-1H-imidazol-2-yl)acetanilide dihydrochloride

Example 53

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[(1-(4-phenylbenzyl)-1H-imidazol-2-yl)acetanilide dihydrochloride

Example 54

(R)-2-[1-(2-Chlorobenzyl)-1H-imidazol-2-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 55

(R)-2-[1-(3-Chlorobenzyl)-1H-imidazol-2-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 56

(R)-2-[1-(3,4-Dichlorobenzyl)-1H-imidazol-2-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 57

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[(1-(2-pyridyl)methyl-1H-imidazol-2-yl)acetanilide dihydrochloride

The compound of Example 58 was prepared by the same manner as in Example 1.

Example 58

(R)-2-(2-aminopyridin-6-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

[0108]

Example 59

To a solution of tert-butyl (R)-N-[2-[4-[[2-(2-aminothiazol-4-yl)-2-oxoacetyl]amino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate in 30 ml of methanol was added 130 mg of sodium borohydride at room temperature. The reaction mixture was stirred at room temperature for three hours, and the solvent was evaporated *in vacuo*. The residue was dissolved in 5 ml of methanol, and to this reaction solution was added 10 ml of a solution of 4N hydrogen chloride-ethyl acetate. The reaction solution was stirred at room temperature for eight hours and the solvent was evaporated *in vacuo*. The residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 5/1). The resulting residue was purified by reversed phase column chromatography (eluent: water/methanol = 2/1) to give 77 mg of (R)-2-(2-aminothiazol-4-yl)-2-hydroxy-4'-[2-(2-hydroxy-2-phenylethyl)-amino]acetanilide hydrochloride.

[0109]

Example 60

To 349 mg of tert-butyl (R)-N-[2-[4-[[2-(2-benzyloxypyridin-6-yl)acetyl]amino]phenyl]ethyl]-N-(2-hydroxy-2-phenylethyl)carbamate were added 478 mg of pentamethylbenzene

and 5 ml of trifluoroacetic acid successively. The reaction solution was stirred at room temperature for four hours, and the solvent was evaporated *in vacuo*. To the residue were added water and potassium carbonate to make the solution basic, and the aqueous phase was extracted with a mixed solvent of chloroform and tetrahydrofuran. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated *in vacuo*. The residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 10/1 → 5/1). To an ethanolic solution of the resulting residue was added 100 μl of a 4N hydrogen chloride-ethyl acetate solution, and then the solvent was evaporated *in vacuo*. The resulting crude crystals were recrystallized from ethanol-ethyl acetate to give 65 mg of (R)-2-(2-benzyloxypyridin-6-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride.

[0110]

The compounds of Examples 61 to 76, 83 and 85 were prepared by the same manner as in Example 1; and the compounds of Examples 77 to 82 were prepared by the same manner as in Example 41.

Example 61

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(2-methylpropyl-1H-imidazol-2-yl)acetanilide dihydrochloride

Example 62

(R)-2-[1-(2-Fluorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 63

(R)-2-[1-(3-Fluorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 64

(R)-2-[1-(2,4-Difluorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 65

(R)-2-[1-(2,6-Difluorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 66

(R)-2-[1-(3,5-Difluorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 67

(R)-2-[1-(2,5-Difluorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 68

(R)-2-[1-(3,4-Difluorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 69

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(2,3,6-trifluorobenzyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

Example 70

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(2,4,5-trifluorobenzyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

[0111]

Example 71

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(3,4,5-trifluorobenzyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

Example 72

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(2,3,4,5,6-pentafluorobenzyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

Example 73

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(3-iodobenzyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

Example 74

(R)-2-[1-(2,6-Dichlorobenzyl)-1H-imidazol-2-yl]-4'-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide hydrochloride

Example 75

(R)-2-[1-(4-Cyanobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 76

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(quinolin-2-yl)-1H-imidazol-2-yl]acetanilide trihydrochloride

Example 77

(R)-2-[1-(2-Chloro-6-fluorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide

Example 78

(R)-2-[1-(2-Chloro-4-fluorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide

Example 79

(R)-2-[1-(2,5-Dichlorobenzyl)-1H-imidazol-2-yl]-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 80

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(2,3,4-trifluorobenzyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

[0112]

Example 81

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-(4-methoxycarbonylbenzyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

Example 82

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[1-[(piperidine-1-carbonyl)benzyl]-1H-imidazol-2-yl]acetanilide dihydrochloride

Example 83

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(1-pyrazolyl)acetanilide hydrochloride

Example 84

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(1,2,4-triazol-1-yl)acetanilide dihydrochloride

Example 85

(R)-2-(2-Aminobenzimidazol-1-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

[0113]

Example 86

To a solution of 20.1 g of 4'-[2-[N-benzyl-N-(2-hydroxy-2-phenylethyl)amino]ethyl]-2-(2-pyridyl)acetanilide in 400 ml of methanol was added 5.96 g of 10% palladium-carbon. The reaction solution was stirred for six hours in a hydrogen atmosphere under atmospheric pressure. Insoluble matters were filtered off using Celite and the filtrate was concentrated *in vacuo*. To a methanolic solution of the resulting residue was

added 10.8 ml of a 4N hydrogen chloride-ethyl acetate solution, and the solvent was evaporated *in vacuo*. The resulting crude crystals were recrystallized from methanol-ethanol to give (R)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]-2-(2-pyridyl)acetanilide hydrochloride.

[0114]

The compounds of 87 to 90 were prepared by the same manner as in Example 86.

Example 87

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(3-pyridyl)acetanilide hydrochloride

Example 88

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(4-pyridyl)acetanilide hydrochloride

Example 89

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-3-(2-pyridyl)propionanilide hydrochloride

Example 90

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-[(1-phenylethyl)-1H-imidazol-2-yl]acetanilide dihydrochloride

[0115]

Example 91

(R)-2-(1H-Benzimidazol-2-yl)-4'-[4-[2-[N-benzyl-N-(2-hydroxy-2-phenylethyl)amino]ethyl]phenyl]acetanilide (240 mg) was dissolved in 30 ml of ethanol, then 170 mg of 10%

palladium-carbon was added thereto and the mixture was stirred for nine hours in a hydrogen atmosphere under atmospheric pressure. The catalyst was filtered off, the solvent was evaporated *in vacuo*, and the residue was washed with ethanol-ethyl acetate to give 200 mg of (R)-2-(1H-benzimidazol-2-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide.

[0116]

The compounds of Examples 92 and 93 were prepared by the same manner as in Example 86.

Example 92

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(3-methylpyridin-2-yl]acetanilide hydrochloride

Example 93

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(2-pyrazinyl)acetanilide hydrochloride

[0117]

Example 94

(R)-4'-[4-[2-[N-Benzyl-N-(2-hydroxy-2-phenylethyl)-amino]ethyl]phenyl]-2-(1-benzyl-1H-imidazol-2-yl)acetanilide (350 mg) was dissolved in 20 ml of ethanol, then 130 mg of 10% palladium-carbon was added thereto, and the mixture was stirred for 17.5 hours in a hydrogen atmosphere under atmospheric pressure. The catalyst was filtered off, the solvent was evaporated *in vacuo*, and the residue was purified

by silica gel column chromatography (eluent: chloroform/methanol/ concentrated aqueous ammonia = 200/10/1). The resulting oily substance was dissolved in methanol, and 280 µl of a 4N hydrogen chloride-ethyl acetate solution was added thereto. The mixture was filtered after adding active carbon was added thereto, and the solvent was evaporated *in vacuo* to give 200 mg of (R)-2-(1-benzyl-1H-imidazol-2-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride.

[0118]

The compounds of Examples 95 and 97 were prepared by the same manner as in Example 91; the compounds of Examples 98 and 100 were prepared by the same manner as in Example 94; and the compounds of Examples 99 and 101 to 103 were prepared by the same manner as in Example 86.

Example 95

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(4-methyl-2-pyridyl)acetanilide

Example 96

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(5-methyl-2-pyridyl)acetanilide

Example 97

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(6-methyl-2-pyridyl)acetanilide

Example 98

4'-[(R)-2-[((R)-Hydroxy-2-phenylethyl)amino]propyl]-2-(2-pyridyl)acetanilide hydrochloride

Example 99

4'-[(S)-2-[((R)-Hydroxy-2-phenylethyl)amino]propyl]-2-(2-pyridyl)acetanilide hydrochloride

Example 100

2-(1-Benzyl-1H-imidazol-2-yl)-4'-[(S)-2-[((R)-2-hydroxy-2-phenylethyl)amino]propyl]acetanilide hydrochloride

Example 101

4'-[2-[[2-Hydroxy-2-(2-fluorophenyl)ethyl]amino]ethyl]-2-(2-pyridyl)acetanilide hydrochloride

Example 102

4'-[2-[[2-Hydroxy-2-(3-fluorophenyl)ethyl]amino]ethyl]-2-(2-pyridyl)acetanilide hydrochloride

Example 103

4'-[2-[[2-Hydroxy-2-(4-fluorophenyl)ethyl]amino]ethyl]-2-(2-pyridyl)acetanilide hydrochloride

[0119]

Example 104

To a solution of 805 mg of 4'-cyanomethyl-2-(2-pyrimidinyl)acetanilide in 30 ml of tetrahydrofuran were added 30 ml of an ethanolic solution of a Raney nickel and 3 ml of concentrated aqueous ammonia. The reaction solution was stirred for four hours in a hydrogen atmosphere under atmospheric pressure, then insoluble matters were filtered off

using Celite, and the solvent was evaporated. To the resulting residue were added 10 ml of 2-propanol, 300 mg of (R)-styrene oxide and 2 ml of methanol successively. The reaction mixture was heated to reflux for ten hours, and the solvent was evaporated. The residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 10/1). To a methanolic solution of the resulting residue was added 150 µl of 4N hydrogen chloride-ethyl acetate solution, and the solvent was evaporated *in vacuo*. The resulting residue was crystallized from methanol-ethanol-ethyl acetate and then recrystallized from ethanol-diethyl ether to give 160 mg of (R)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]-2-(2-pyrimidinyl]acetanilide hydrochloride.

[0120]

The compounds of Examples 105 to 108 were prepared by the same manner as in Example 104; and the compound of Example 109 was prepared by the same manner as in Example 91.

Example 105

(R)-4'-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]-2-(2-quinolyl)acetanilide hydrochloride

Example 106

(R)-4'-[2-[[2-Hydroxy-2-(3-chlorophenyl)ethyl]amino]ethyl]-2-(2-pyridyl)acetanilide hydrochloride

Example 107

4'-[2-[[2-Hydroxy-2-(3-pyridyl)ethyl]amino]ethyl]-2-(2-pyridyl)acetanilide hydrochloride

Example 108

(R)-2-[1-(4-Chlorobenzyl)-1H-benzimidazol-2-yl]-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide dihydrochloride

Example 109

(R)-2-(4,6-Dimethyl-2-pyridyl)-4'-[2-[(2-hydroxy-2-phenyl-ethyl)amino]ethyl]acetanilide

[0121]

Example 110

To 4'-(3-aminopropyl)-2-(2-pyridyl)acetanilide were added 10 ml of 2-propanol and 600 mg of (R)-styrene oxide successively. The reaction mixture was heated to reflux for four hours, and the solvent was evaporated. The residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 30/1 → 10/1). To a methanolic solution of the resulting residue was added 100 μl of a 4N hydrogen chloride-ethyl acetate solution, and the solvent was evaporated *in vacuo*. The resulting crude crystals were recrystallized from ethanol-diethyl ether to give 71 mg of (R)-4'-[3-[(2-hydroxy-2-phenylethyl)amino]propyl]-2-(2-pyridyl)acet-anilide hydrochloride.

[0122]

Example 111

To a solution of 3.62 g of tert-butyl N-[2-[4-[[2-(2-pyridyl)acetyl]amino]phenoxy]ethyl]carbamate in 30 ml of methanol was added 50 ml of a 4N hydrochloride-ethyl acetate solution. After the reaction solution was stirred at room temperature for eight hours, the solvent was evaporated *in vacuo*. To the residue were added an aqueous solution of sodium hydrogen carbonate and potassium carbonate to adjust to pH about 12. The resulting aqueous phase was extracted with a mixed solvent of chloroform and tetrahydrofuran. The organic layer was dried over anhydrous magnesium sulfate and concentrated, the resulting residue was dissolved in 40 ml of methanol, and 1.02 g of (R)-styrene oxide was added thereto. After the reaction solution was heated to reflux for 26 hours, the solvent was evaporated *in vacuo*. The resulting residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 30/1 → 10/1) and dissolved in methanol, 0.59 ml of a 4N hydrogen chloride-ethyl acetate solution was added, and the solvent was evaporated *in vacuo*. The resulting crude crystals were recrystallized from methanol-ethanol to give 320 mg of (R)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethoxy]-2-(2-pyridyl)acetanilide hydrochloride

[0123]

Example 112

To a solution of 490 mg of tert-butyl N-[1,1-dimethyl-2-[4-[[2-(2-pyridyl)acetyl]amino]phenyl]ethyl]-

carbamate in 10 ml of methanol was added 30 ml of a 4N hydrochloride-ethyl acetate solution. After the reaction solution was stirred at room temperature for eight hours, the solvent was evaporated *in vacuo*. To the residue were added an aqueous solution of sodium hydrogen carbonate and potassium carbonate to adjust to pH about 12. The resulting aqueous phase was extracted with a mixed solvent of chloroform and tetrahydrofuran. The organic layer was dried over anhydrous magnesium sulfate and concentrated, the resulting residue was dissolved in 2 ml of 2-propanol and 2 ml of methanol, and 120 mg of (R)-styrene oxide was added thereto. After the reaction solution was heated to reflux for 24 hours, the solvent was evaporated *in vacuo*. The resulting residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 30/1 → 5/1) and dissolved in methanol, 0.1 ml of a 4N hydrogen chloride-ethyl acetate solution was added, and the solvent was evaporated *in vacuo*. The resulting residue was purified by silica gel column chromatography (eluent: chloroform/methanol = 5/1) and a reversed phase column chromatography (eluent: water/methanol = 2/1 → 1/1) to give 35 mg of (R)-4'-[2,2-dimethyl-2-[(2-hydroxy-2-phenylethyl)amino]ethyl]-2-(2-pyridyl)acetanilide hydrochloride

[0124]

The compound of Example 113 was prepared by the same manner as in Example 1.

Example 113

(R)-1-[4-[2-[(2-Hydroxy-2-phenylethyl)amino]ethyl]phenyl]-3-(2-pyridyl)urea dihydrochloride

[0125]

As hereunder, physical and chemical properties of the compounds of the Referential Examples are given in Tables 1 to 13 and those of the compounds of the Examples are given in Tables 14 to 25.

The symbols in the tables have the following meanings.

Rex.: Referential Example No.

Ex.: Example No.

DATA: Physico-chemical properties

NMR: Nucleomagnetic resonance spectrum (TMS internal standard; DMSO-d_6 was used as a solvent unless otherwise specified)

mp: melting point

dec: decomposition

MS (m/z): mass spectrographic data (m/z)

[0126]

[Table 1]

Rex.	D A T A
1	NMR ($CDCl_3$) δ: 1.28(3H,t,J=7.2Hz), 3.88(2H,s), 4.21(2H,q,J=7.2Hz), 7.56-7.71(1H,m), 8.53-8.56(1H,m), 8.60-8.62(1H,m)
2	NMR ($CDCl_3$) δ: 1.22(3H,t,J=7.1Hz), 3.95(2H,s), 4.12(2H,q,J=7.1Hz), 5.39(2H,s), 7.00(2H,d,J=8.7Hz), 7.17-7.30(5H,m), 7.78(1H,dd,J=7.1, 2.0Hz)
3	NMR δ: 1.22(3H,t,J=6.9Hz), 4.16(2H,q,J=6.9Hz), 4.26(2H,s), 7.62(2H,s)
4	NMR δ: 4.16(2H,s), 7.61(2H,s)
5	NMR ($CDCl_3$) δ: 3.89(2H,s), 7.20-7.32(2H,m), 7.63-7.71(1H,m), 11.03(1H,brs)
6	NMR δ: 2.11(3H,s), 3.58(2H,s), 6.91(1H,s), 11.90-12.50(2H,m)
7	NMR δ: 3.56(2H,s), 5.48(2H,s), 7.13(2H,d,J=6.9Hz), 7.24-7.39(3H,m), 12.90(1H,s)
8	NMR δ: 1.46(6H,s), 6.64(1H,s), 9.00(1H,brs)
9	NMR ($CDCl_3$) δ: 3.70(2H,s), 3.73(3H,s), 6.81(1H,s)
10	NMR δ: 3.66(2H,s), 7.11(1H,s), 8.28(4H,brs), 12.46(1H,brs)
11	NMR ($CDCl_3$) δ: 1.34(3H,t,J=7.2Hz), 3.77(2H,s), 4.28(2H,q,J=7.2Hz), 6.59(1H,s), 6.98-7.22(3H,m), 7.39-7.49(1H,m)
12	NMR δ: 3.58(2H,s), 6.72(1H,s), 6.73-6.79(1H,m), 7.22-7.37(2H,m), 7.64-7.71(1H,m), 10.59(1H,brs)
13	NMR ($CDCl_3$) δ: 1.21(3H,t,J=7.2Hz), 2.16(3H,s), 3.67(2H,s), 4.11(2H,q,J=7.2Hz)
14	NMR δ: 2.16(3H,s), 3.60(2H,s), 9.16(2H,brs)
15	NMR ($CDCl_3$) δ: 3.78(3H,s), 3.91(2H,s), 4.34(2H,s), 7.20-7.39(5H,m)
16	NMR δ: 3.74(2H,s), 4.33(2H,s), 7.20-7.39(5H,m)
17	NMR ($CDCl_3$) δ: 1.23(3H,t,J=7.2Hz), 3.75(2H,s), 4.13(2H,q,J=7.2Hz), 5.10(2H,s), 6.84(1H,d,J=1.2Hz), 7.00-7.12(5H,m)
18	NMR δ: 4.33(2H,s), 5.43(2H,s), 7.21-7.27(2H,m), 7.42-7.47(2H,m), 7.68-7.69(2H,m)
19	NMR ($CDCl_3$) δ: 1.23(3H,t,J=7.3Hz), 3.73(2H,s), 4.12(2H,q,J=7.3Hz), 5.11(2H,s), 6.84(1H,d,J=1.4Hz), 7.02-7.06(3H,m), 7.30-7.34(2H,m)
20	NMR δ: 4.32(2H,s), 5.45(2H,s), 7.39(2H,d,J=8.8Hz), 7.46(2H,d,J=8.8Hz), 7.70(2H,s), 14.00(1H,brs)
21	NMR ($CDCl_3$) δ: 1.23(3H,t,J=7.1Hz), 3.74(2H,s), 4.12(2H,q,J=7.1Hz), 5.12(2H,s), 6.87(1H,d,J=1.4Hz), 6.96-6.99(1H,m), 7.04(1H,d,J=1.4Hz), 7.08(1H,brs), 7.25-7.31(2H,m)
22	NMR δ: 4.35(2H,s), 5.46(2H,s), 7.32-7.35(1H,m), 7.43-7.44(2H,m), 7.48(1H,brs), 7.70(1H,d,J=1.8Hz), 7.72(1H,d,J=1.8Hz)
23	NMR ($CDCl_3$) δ: 1.22(3H,t,J=7.1Hz), 3.77(2H,s), 4.06(2H,q,J=7.1Hz), 5.23(2H,s), 6.78(1H,dd,J=7.5, 1.5Hz), 6.86(1H,d,J=1.5Hz), 7.05(1H,d,J=1.5Hz), 7.19-7.30(2H,m), 7.41(1H,dd,J=7.5, 1.5Hz)
24	NMR δ: 4.32(2H,s), 5.55(2H,s), 7.15-7.73(6H,m)

[0127]

[Table 2]

Rex.	D A T A
25	NMR (CDCl3) δ: 1.24(3H,t,J=7.1Hz), 3.74(2H,s), 4.15(2H,q,J=7.1Hz), 5.10 (2H,s), 6.85(1H,d,J=1.5Hz), 6.94(1H,dd,J=8.4, 2.1Hz), 7.04(1H,d,J=1.5Hz), 7.20(1H,d,J=2.1Hz), 7.42(1H,d,J=8.4Hz)
26	NMR δ: 4.38(2H,s), 5.48(2H,s), 7.39(1H,dd,J=8.4, 1.8Hz), 7.67-7.72(3H,m), 7.76(1H,d,J=2.4Hz)
27	NMR (CDCl3) δ: 1.13(3H,t,J=6.7Hz), 4.01(2H,q,J=6.7Hz), 4.42(2H,s), 5.46 (2H,s), 7.31(2H,d,J=8.4Hz), 7.60(2H,d,J=8.4Hz), 7.73(1H,d,J=1.5Hz), 7.77(1H,d,J=1.5Hz)
28	NMR δ: 4.31(2H,s), 5.43(2H,s), 7.32(2H,d,J=8.4Hz), 7.61(2H,d,J=8.4Hz), 7.70(2H,s)
29	NMR (CDCl3) δ: 1.23(3H,t,J=6.9Hz), 3.73(2H,s), 4.12(2H,q,J=6.9Hz), 5.08 (2H,s), 6.83-6.86(3H,m), 7.02(1H,d,J=1.5Hz), 7.67(2H,d,J=8.4Hz)
30	NMR δ: 4.31(2H,s), 5.41(2H,s), 7.16(2H,d,J=8.3Hz), 7.55-7.61(2H,m), 7.7 6(2H,d,J=8.3Hz)
31	NMR (CDCl3) δ: 1.22(3H,t,J=7.0Hz), 3.74(2H,s), 4.10(2H,q,J=7.0Hz), 5.21 (2H,s), 6.86(1H,d,J=1.4Hz), 7.05(1H,d,J=1.4Hz), 7.20(2H,d,J=9.5Hz), 7.60(2H,d,J=9.5Hz)
32	NMR δ: 4.32(2H,s), 5.57(2H,s), 7.54(2H,d,J=8.0Hz), 7.70-7.75(2H,m), 7.7 7(2H,d,J=8.0Hz)
33	NMR (CDCl3) δ: 1.20-1.26(9H,m), 2.89(1H,sep.J=7.2Hz), 3.75(2H,s), 4.11(2H,q,J=6.9Hz), 5.09(2H,s), 6.86(1H,d,J=1,2Hz), 7.02(2H,d,J=7.2Hz), 7.19(2H,d,J=7.2Hz), 7.26(1H,d,J=1.2Hz)
34	NMR δ: 1.18(6H,d,J=6.6Hz), 2.88(1H,sep,6.6Hz), 4.32(2H,s), 5.38(2H,s), 7.27(2H,s), 7.66-7.68(4H,m)
35	NMR (CDCl3) δ: 1.17(3H,t,J=7.2Hz), 3.43(2H,s), 4.03(2H,q,J=7.2Hz), 4.99 (2H,s), 6.70(1H,d,J=1.2Hz), 6.94(1H,d,J=1.2Hz), 7.03-7.44(9H,m)
36	NMR δ: 3.91(2H,s), 5.38(2H,s), 7.21(1H,d,J=7.2Hz), 7.29-7.50(9H,m), 7.5 9(1H,d,J=1.5Hz)
37	NMR (CDCl3) δ: 1.20(3H,t,7.3Hz), 3.76(2H,s), 4.09(2H,q,J=7.3Hz), 5.29(2 H,s), 6.92(1H,d,J=1.4Hz), 7.05(1H,d,J=1.4Hz), 7.21-7.26(1H,m), 7.46-7.52(3H,m), 7.75-7.85(3H,m)
38	NMR δ: 4.37(2H,s), 5.61(2H,s), 7.45-7.50(1H,m), 7.52-7.60(2H,m), 7.70-7. 76(2H,m), 7.80-7.90(4H,m)
39	NMR (CDCl3) δ: 1.22(3H,t,J=7.1Hz), 3.82(2H,s), 4.11(2H,q,J=7.1Hz), 5.26 (2H,s), 6.93(1H,d,J=7.8Hz), 6.96(1H,d,J=1.4Hz), 7.05(1H,d,J=1.4Hz), 7.23(1H,dd,J=6.8, 5.0Hz), 7.66(1H,td,J=7.8, 1.9Hz), 8.58(1H,d,J=5.0Hz)
40	NMR δ: 4.35(2H,s), 5.70(2H,s), 7.53(1H,dd,J=7.5, 4.8Hz), 7.58(1H,d,J=7.5 Hz), 7.71(1H,d,J=1.9Hz), 7.82(1H,d,J=1.9Hz), 8.03(1H,td,J=4.8, 1.9Hz), 8. 61(1H,d,J=4.2Hz)
41	NMR (CDCl3) δ: 1.26(3H,dt,J=7.3, 1.4Hz), 1.70(3H,s), 3.77(2H,d,J=1.3Hz), 4.13(2H,dq,J=7.3, 1.4Hz), 4.45(2H,s), 4.64(1H,s), 4.90-4.95(1H,m), 6.85-7.28(2H,m)

[0128]

[Table 3]

Rex.	D A T A
42	NMR δ: 1.66(3H,s), 4.21(2H,s), 4.73(1H,s), 4.81(2H,s), 4.99(1H,s), 7.66(1H,d,J=1.8Hz), 7.71(1H,d,J=1.8Hz)
43	NMR ($CDCl_3$) δ: 1.26(3H,t,J=7.2Hz), 3.63(2H,d,J=0.6Hz), 4.17(2H,q,J=7.2Hz), 5.07(2H,s), 6.87(1H,d,J=1.1Hz), 7.15-7.18(2H,m), 7.31-7.37(3H,m), 7.46(1H,d,J=1.1Hz)
44	NMR δ: 3.78(2H,s), 5.42(2H,s), 7.38-7.44(6H,m), 7.58(1H,brs), 9.26(1H,brs)
45	NMR ($CDCl_3$) δ: 1.26(3H,t,J=7.2Hz), 3.64(2H,d,J=0.6Hz), 4.17(2H,q,J=7.2Hz), 5.18(2H,s), 6.91(1H,s), 6.99(1H,dd,J=8.4, 2.0Hz), 7.21-7.31(2H,m), 7.41(1H,dd,J=8.4, 2.0Hz), 7.49(1H,d,J=1.5Hz)
46	NMR δ: 3.79(2H,s), 5.43(2H,s), 7.42-7.58(6H,m), 9.26(1H,brs)
47	NMR ($CDCl_3$) δ: 1.26(3H,t,J=7.1Hz), 3.64(2H,d,J=0.6Hz), 4.17(2H,q,J=7.1Hz), 5.05(2H,s), 6.87(1H,s), 7.02-7.05(1H,m), 7.15(1H,d,J=0.9Hz), 7.28-7.30(2H,m), 7.47(1H,d,J=0.9Hz)
48	NMR δ: 3.78(2H,s), 5.54(2H,s), 7.39-7.47(4H,m), 7.58(1H,brs), 7.61(1H,brs), 9.27(1H,brs)
49	NMR ($CDCl_3$) δ: 1.26(3H,t,J=7.1Hz), 3.63(2H,s), 4.17(2H,q,J=7.1Hz), 5.04(2H,s), 6.69(1H,s), 7.08(1H,s), 7.11(1H,s), 7.31(1H,t,J=2.3Hz), 7.34(1H,t,J=2.3Hz), 7.45(1H,d,J=1.2Hz)
50	NMR δ: 3.78(2H,s), 5.41(2H,s), 7.45-7.52(5H,m), 7.58(1H,brs), 9.20(1H,brs)
51a	NMR ($CDCl_3$) δ: 1.22(3H,t,J=7.2Hz), 3.78(2H,s), 4.12(2H,q,J=7.2Hz), 5.37(2H,s), 7.15-7.21(2H,m), 7.28-7.39(3H,m), 7.90(1H,s)
51b	NMR ($CDCl_3$) δ: 1.26(3H,t,J=7.2Hz), 3.81(2H,s), 4.20(2H,q,J=7.2Hz), 5.30(2H,s), 7.23-7.29(2H,m), 7.34-7.39(3H,m), 7.96(1H,s)
52	NMR δ: 4.04(3H,s), 5.41(2H,s), 7.24-7.38(5H,m), 8.49(1H,s)
53	NMR δ: 3.62(3H,s), 5.37(2H,s), 7.25-7.41(5H,m), 8.65(1H,s)
54a	NMR ($CDCl_3$) δ: 1.25(3H,t,J=7.2Hz), 3.85(2H,s), 4.16(2H,q,J=7.2Hz), 5.59(2H,s), 7.07(2H,t,J=8.4Hz), 7.20-7.27(2H,m)
54b	NMR ($CDCl_3$) δ: 1.25(3H,t,J=7.2Hz), 3.95(2H,s), 4.19(2H,q,J=7.2Hz), 5.72(2H,s), 7.06(2H,t,J=8.4Hz), 7.35-7.39(2H,m)
55	NMR δ: 4.19(2H,s), 5.63(2H,s), 7.10-7.50(4H,m), 13.10(1H,brs)
56	NMR δ: 3.93(2H,s), 5.91(2H,s), 7.23(2H,t,J=8.7Hz), 7.43-7.47(2H,m), 12.79(2H,brs)
57a	NMR ($CDCl_3$) δ: 1.26(3H,t,J=7.0Hz), 3.89(2H,s), 4.17(2H,q,J=7.0Hz), 5.57(2H,s), 7.00-7.10(1H,m), 7.35-7.47(2H,m)
57b	NMR ($CDCl_3$) δ: 1.26(3H,t,J=7.0Hz), 3.96(2H,s), 4.20(2H,q,J=7.0Hz), 5.71(2H,s), 7.20-7.22(1H,m), 7.44-7.48(2H,m)
58	NMR δ: 4.23(2H,s), 5.66(2H,s), 7.32-7.35(1H,m), 7.64-7.67(2H,m), 7.70(2H,s), 13.14(1H,brs)

[0129]

[Table 4]

Rex.	D A T A
59	NMR δ: 3.95(2H,s), 5.97(2H,s), 7.33-7.39(1H,m), 7.66-7.71(2H,m), 12.81(1H,brs)
60	NMR ($CDCl_3$) δ: 1.19(3H,t,J=7.3Hz), 3.75(2H,s), 4.12(2H,q,J=7.3Hz), 7.06(1H,d,J=1.5Hz), 7.12(1H,d,J=1.5Hz), 7.32-7.52(5H,m)
61	NMR δ: 4.16(2H,s), 7.55-7.70(5H,m), 7.88-7.91(1H,m), 7.98-8.00(1H,m)
62	NMR ($CDCl_3$) δ: 1.23(3H,t,J=6.8Hz), 3.75(2H,s), 4.12(2H,q,J=6.8Hz), 5.28(2H,s), 6.87(1H,d,J=1.2Hz), 7.08(1H,d,J=1.2Hz), 7.26(2H,d,J=8.4Hz), 8.22(2H,d,J=8.4Hz)
63	NMR δ: 4.32(2H,s), 5.64(2H,s), 7.58(2H,d,J=8.9Hz), 7.73-7.78(2H,m), 8.25(2H,d,J=8.9Hz), 14.00(1H,brs)
64	NMR ($CDCl_3$) δ: 1.25(3H,t,J=6.9Hz), 3.02(2H,t,J=6.9Hz), 3.51(2H,s), 4.09-4.19(4H,m), 6.81(1H,d,J=1.5Hz), 6.96(1H,d,J=1.5Hz), 7.03-7.32(5H,m)
65	NMR δ: 3.08(2H,t,J=7.5Hz), 4.14(2H,s), 4.44(2H,t,J=7.5Hz), 7.20-7.35(5H,m), 7.64(1H,d,J=1.5Hz), 7.68(1H,d,J=1.5Hz)
66	NMR ($CDCl_3$) δ: 2.09(3H,s), 2.30(3H,s), 4.99(2H,s), 6.72(1H,s), 6.88-7.04(4H,m)
67	NMR ($CDCl_3$) δ: 1.21(3H,t,J=6.9Hz), 2.09(3H,d,J=0.6Hz), 3.69(2H,s), 4.08(2H,q,J=6.9Hz), 5.09(2H,s), 6.80(1H,d,J=0.6Hz), 6.86-7.04(4H,m)
68	NMR δ: 2.12(3H,s), 4.31(2H,s), 5.45(2H,s), 7.18-7.28(4H,m), 7.50(1H,s)
69	NMR ($CDCl_3$) δ: 2.18(3H,d,J=2.0Hz), 2.30(3H,s), 4.94(2H,s), 6.51(1H,d,J=1.5Hz), 6.88-7.04(4H,m)
70	NMR ($CDCl_3$) δ: 1.23(3H,t,J=7.2Hz), 2.19(3H,d,J=0.6Hz), 3.71(2H,s), 4.12(2H,q,J=7.2Hz), 5.03(2H,s), 6.54(1H,d,J=0.6Hz), 7.00-7.12(4H,m)
71	NMR δ: 2.24(3H,s), 4.27(2H,s), 5.35(2H,s), 7.21-7.45(5H,m)
72	NMR ($CDCl_3$) δ: 1.26(3H,t,J=6.8Hz), 3.87(2H,s), 4.18(2H,q,J=6.8Hz), 5.36(2H,s), 6.73(1H,d,J=6.8Hz), 6.85(1H,d,J=6.8Hz), 7.20-7.65(6H, m)
73	NMR ($CDCl_3$) δ: 3.41(2H,s), 5.40(2H,s), 6.70-7.00(2H,s), 7.20-7.70(6H,m)
74	NMR ($CDCl_3$) δ: 1.25(3H,t,J=7.2Hz), 1.48(9H,s), 3.69(2H,s), 4.17(2H,q,J=7.2Hz), 6.93(1H,d,J=7.9Hz), 7.58-7.65(1H,m), 7.82(1H,d,J=8.3Hz)
75	NMR ($CDCl_3$) δ: 1.51(9H,s), 3.68(2H,s), 6.80-7.00(1H,s), 7.50-7.90(2H,m)
76	NMR ($CDCl_3$) δ: 1.30-2.20(4H,s), 2.60-3.10(2H,s), 3.70-4.00(1H,m), 7.00-8.00(2H,s), 8.20-8.60(1H,m)
77	NMR ($CDCl_3$) δ: 2.75(1H,dd,J=12.4, 8.8Hz), 2.85-3.04(5H,m), 4.70(1H,dd,J=8.8, 3.7Hz), 7.24-7.40(7H,m), 8.10-8.20(2H,m)
78	NMR ($CDCl_3$) δ: 1.44(9H,s), 2.75-3.10(2H,m), 3.20-3.70(4H,m), 4.93(1H,br), 7.25-7.40(7H,m), 8.14(2H,d,J=8.4Hz)
79	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.55-2.80(2H,m), 3.20-3.40(2H,m), 3.45-3.65(2H,m), 4.87(1H,m), 6.57-6.65(2H,m), 6.83-7.04(2H,m), 7.25-7.40(5H,m)
80	NMR ($CDCl_3$) δ: 2.87(2H,dt,J=6.6, 2.4Hz), 3.44-3.65(3H,m), 4.97(1H,s), 6.27(1H,brs), 7.16(2H,d,J=8.9Hz), 7.29-7.37(5H,m), 8.05(2H,d,J=8.9Hz)

[0130]

[Table 5]

Rex.	D A T A
81	NMR δ: 3.04(1H,dd,J=12.3, 10.2Hz), 3.16-3.29(5H,m), 5.10(1H,brd,J=9.9Hz), 6.21(1H,brd,J=3.6Hz), 7.29-7.37(1H,m), 7.39-7.41(4H,m), 7.57(2H,d,J=8.6Hz), 8.21(2H,d,J=8.6Hz), 9.15(1H,brs),
82	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.62-2.93(2H,m), 3.14-3.58(4H,m), 4.35(1H,brs), 4.90(1H,br), 7.06-7.40(7H,m), 7.45-7.50(1H,m), 7.67-7.72(2H,m), 7.90(1H,dt,J=2.0, 8.0Hz), 8.25-8.31(1H,m), 8.58-8.63(1H,m), 9.98(1H,brs)
83	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.90(2H,m), 3.15-3.70(4H,m), 4.32(1H,brs), 4.85-4.94(1H,m), 7.05-7.46(8H,m), 7.55-7.61(2H,m), 8.16-8.23(1H,m), 8.75(1H,br), 9.05(1H,br)
84	NMR ($CDCl_3$) δ: 1.49(9H,s), 2.64-2.90(2H,m), 3.16-3.60(4H,m), 4.38(1H,brs), 4.91(1H,br), 7.10-7.42(7H,m), 7.55(1H,dd,J=8.0, 4.4Hz), 7.74(1H,t,J=8.0Hz), 7.77-7.84(2H,m), 8.01(1H,d,J=8.0, 1.2Hz), 8.34(1H,d,J=8.4, 1.6Hz), 8.96(1H,d,J=7.6, 1.6Hz), 9.02(1H,d,J=4.4, 2.0Hz), 13.61(1H,brs)
85	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.90(2H,m), 3.20-3.55(4H,m), 4.35(1H,brs), 4.90(1H,br), 7.06-7.18(3H,m), 7.23-7.56(9H,m), 7.66-7.77(2H,m), 8.62(1H,d,J=4.0Hz)
86	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.85(2H,m), 3.15-3.55(4H,m), 4.31(1H,brs), 4.88(1H,br), 7.01-7.20(2H,m), 7.22-7.56(9H,m), 7.90(1H,d,J=8.0Hz), 8.05(1H,d,J=8.0Hz), 9.54(1H,brs)
87	NMR ($CDCl_3$) δ: 1.45(9H,s), 2.60-2.85(2H,m), 3.10-3.50(4H,m), 3.80(2H,s), 4.40(1H,brs), 4.80-4.90(1H,m), 6.71(1H,s), 6.97-7.14(2H,m), 7.22-7.49(8H,m), 8.01(1H,s), 8.48(1H,brs)
88	NMR ($CDCl_3$) δ: 1.34(9H,s), 2.89(3H,s), 3.06-3.36(6H,m), 3.73(2H,s), 4.72(1H,s), 7.06-7.57(10H,m), 10.10(1H,s)
89	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.52-2.80(2H,m), 3.10-3.60(4H,m), 3.89(2H,s), 4.85-4.95(1H,m), 6.95-7.40(9H,m), 7.49(2H,d,J=8.4Hz), 10.16(1H,brs)
90	NMR ($CDCl_3$) δ: 1.45(9H,s), 2.50-3.50(6H,m), 4.23(2H,s), 4.65-4.75(1H,m), 7.07(2H,d,J=8.0Hz), 7.20-7.80(7H,m), 9.26(1H,brs)
91	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.56-3.40(6H,m), 3.73(2H,s), 4.75-4.91(1H,m), 7.00-7.47(9H,m), 9.15(1H,brs), 12.61(1H,brs)
92	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.90(2H,m), 3.15-3.60(4H,m), 4.27(1H,brs), 4.91(1H,br), 5.31(2H,brs), 7.00-7.50(7H,m), 7.60(2H,d,J=8.0Hz), 8.80(1H,s), 9.12(1H,brs)
93	NMR ($CDCl_3$) δ: 1.45(9H,s), 2.60-2.75(2H,m), 3.10-3.55(4H,m), 3.81(2H,s), 4.81-4.87(1H,m), 6.40-6.55(2H,m), 7.03(2H,d,J=7.3Hz), 7.22-7.45(7H,m), 9.26(1H,s)
94	NMR ($CDCl_3$) δ: 1.44(3H,t,J=7.1Hz), 1.47(9H,s), 2.65-2.80(2H,m), 3.15-3.50(4H,m), 4.04(2H,s), 4.43(2H,q,J=7.1Hz), 4.83-4.90(1H,m), 7.02-7.15(2H,m), 7.30-7.35(5H,m), 7.45(2H,d,J=8.3Hz), 9.21(1H,s)
95	NMR ($CDCl_3$) δ: 1.45(9H,s), 2.60-2.75(2H,m), 3.10-3.50(4H,m), 3.64(2H,s), 4.82-4.91(1H,m), 6.43(1H,s), 6.70-7.44(13H,m), 9.14(1H,brs)

[0131]

[Table 6]

Rex.	D A T A
96	NMR (CDCl3) δ: 1.46(9H,s), 2.60-2.80(2H,m), 3.15-3.55(4H,m), 3.82(2H,s), 4.35(1H,brs), 4.88(1H,br), 6.97-7.16(2H,m), 7.22-7.38(7H,m), 7.42-7.48(2H,m), 7.66(1H,t,J=8.0Hz), 9.18(1H,brs)
97	NMR (CDCl3) δ: 1.46(9H,s), 2.60-2.85(2H,m), 3.15-3.55(4H,m), 3.77(2H,s), 4.33(1H,brs), 4.87(1H,br), 5.64(2H,s), 6.77(1H,d,J=8.4Hz), 6.89(1H,d,J=7.2Hz), 6.94-7.12(2H,m), 7.21-7.41(10H,m), 7.43-7.48(2H,m), 7.59(1H,dd,J=8.4, 7.2Hz), 9.05(1H,brs)
98	NMR (CDCl3) δ: 1.47(9H,s), 1.71(3H,s), 2.60-2.80(2H,m), 3.20-3.60(4H,m), 3.73(2H,s), 4.47(2H,s), 4.56(1H,s), 4.85-4.92(1H,m), 4.94(1H,s), 6.88(1H,s), 7.00-7.20(3H,m), 7.35-7.40(4H,m), 7.48(2H,d,J=8.3Hz), 10.33(1H,brs)
99	NMR (CDCl3) δ: 1.47(9H,s), 2.69(2H,brs), 3.11-3.43(4H,m), 3.61(2H,s), 4.42(1H,brs), 4.88(1H,brs), 5.08(2H,s), 6.80(1H,s), 7.03(2H,brs), 7.17(2H,dd, J=7.5, 2.1Hz), 7.33-7.41(8H,m), 7.45(2H,d,J=8.4Hz), 7.54(1H,d,J=1.2Hz), 9.44(1H,brs)
100	NMR (CDCl3) δ: 1.47(9H,s), 2.68(2H,brs), 3.11-3.43(4H,m), 3.62(2H,s), 4.39(1H,brs), 4.88(1H,brs), 5.19(2H,s), 6.83(1H,s), 7.03-7.06(3H,m), 7.24-7.35(7H,m), 7.42-7.47(3H,m), 7.58(1H,d,J=1.2Hz), 9.41(1H,brs)
101	NMR (CDCl3) δ: 1.47(9H,s), 2.69(2H,brs), 3.11-3.43(4H,m), 3.63(2H,s), 4.37(1H,brs), 4.87(1H,brs), 5.06(2H,s), 6.80(1H,s), 7.03(2H,brs), 7.17(1H,s), 7.30-7.35(8H,m), 7.45(2H,d,J=8.4Hz), 7.55(1H,d,J=1.2Hz), 9.37(1H,brs)
102	NMR (CDCl3) δ: 1.47(9H,s), 2.69(2H,brs), 3.11-3.43(4H,m), 3.62(2H,s), 4.337(1H,brs), 4.87(1H,brs), 5.06(2H,s), 6.78(1H,s), 7.05(2H,brs), 7.11(2H,d, J=8.4Hz), 7.33-7.36(7H,m), 7.45(2H,d,J=8.4Hz), 7.54(1H,brs), 9.38(1H,brs)
103	NMR (CDCl3) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.10-3.50(4H,m), 3.90(2H,s), 4.85-4.95(1H,m), 5.30(2H,s), 6.88(1H,s), 7.00-7.45(12H,m), 7.57(2H,d,J=8.3Hz), 7.70-7.76(1H,m), 7.87-7.96(1H,m), 9.98(1H,brs)
104	NMR (CDCl3) δ: 1.47(9H,s), 2.50-2.70(2H,m), 3.10-3.50(4H,m), 3.70(2H,s), 4.84-4.92(1H,m), 5.12(2H,s), 6.92-7.08(6H,m), 7.26-7.45(9H,m), 10.14(1H,s)
105	NMR (CDCl3) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.10-3.50(4H,m), 3.70(2H,s), 4.85-4.92(1H,m), 5.10(2H,s), 6.91-6.97(4H,m), 7.25-7.47(11H,m), 10.13(1H,brs)
106	NMR (CDCl3) δ: 1.47(9H,s), 2.50-3.00(2H,m), 3.10-3.60(4H,m), 3.82(2H,s), 4.85-4.92(1H,m), 6.83-6.91(3H,m), 7.00-7.20(3H,m), 7.30-7.40(5H,m), 7.51(2H,d,J=8.8Hz), 7.67(2H,d,J=8.3Hz), 9.95(1H,m)
107	NMR (CDCl3) δ: 1.47(9H,s), 2.50-2.70(2H,m), 3.10-3.60(4H,m), 3.70(2H,s), 4.30-4.40(1H,m), 4.88(1H,brs), 5.22(2H,s), 6.88-7.35(9H,m), 7.42(2H,d,J=8.3Hz), 7.59(2H,d,J=8.3Hz), 10.05(1H,brs)
108	NMR (CDCl3) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.10-3.50(4H,m), 4.19(2H,s), 4.80-4.90(1H,m), 5.60(2H,s), 6.93(1H,s), 6.94-7.90(17H,m), 10.05(1H,brs)
109	NMR (CDCl3) δ: 1.47(9H,s), 2.03(3H,s), 2.60-2.70(2H,m), 3.10-3.60(4H,m), 3.66(2H,s), 4.35(1H,brs), 4.87-4.89(1H,m), 5.08(2H,s), 6.84-7.20(7H,m), 7.70-7.90(5H,m), 7.44(2H,d,J=8.3Hz), 10.21(1H,brs)

[0132]

[Table 7]

Rex.	D A T A
110	NMR ($CDCl_3$) δ: 1.48(9H,s), 2.23(3H,s), 2.60-2.80(2H,m), 3.10-3.60(4H,m), 3.68(2H,s), 4.35(1H,brs), 4.85-4.89(1H,m), 5.05(2H,s), 6.60(1H,s), 7.00-7.35(11H,m), 7.44(2H,d,J=8.3Hz), 10.17(1H,brs)
111	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.60-2.90(2H,m), 3.10-3.55(4H,m), 3.89(2H,s), 4.85-4.95(1H,m), 5.66(2H,s), 7.00-7.10(4H,m), 7.50-7.90(9H,m), 8.66(1H,brs)
112	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.60-2.80(2H,m), 3.20-3.50(4H,m), 4.02(2H,s), 4.83-4.91(1H,m), 5.71(2H,s), 7.00-7.51(12H,m), 8.41(1H,brs)
113	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.10-2.30(2H,m), 3.10-3.55(4H,m), 4.02(2H,s), 4.85-4.95(1H,m), 5.73(2H,s), 7.00-7.20(4H,m), 7.30-7.45(9H,m), 8.85(1H,brs)
114	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.60-2.80(2H,m), 3.10-3.60(4H,m), 3.92(2H,s), 4.27(1H,brs), 4.80-4.90(1H,m), 5.65(2H,s), 7.00-7.45(12H,m), 8.47(1H,brs)
115	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.60-3.36(6H,m), 3.98(2H,m), 4.81-4.89(1H,m), 7.02-7.12(2H,m), 7.29-7.50(7H,m), 8.09(1H,brs), 9.24(1H,brs)
116	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.60-3.40(6H,m), 3.88(2H,s), 4.37(2H,s), 4.80-4.95(1H,m), 7.00-7.45(14H,m), 8.02(1H,s)
117	NMR ($CDCl_3$) δ: 1.43(9H,s), 2.20(3H,s), 2.50-3.55(6H,m), 3.67(2H,s), 4.78-4.87(1H,m), 6.71(1H,s), 6.98(2H,d,J=8.5Hz), 7.24-7.45(7H,m), 8.89(1H,brs), 10.38(1H,brs)
118	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.60-2.84(2H,m), 3.00(3H,s), 3.20-3.50(4H,m), 3.71(2H,s), 4.81-4.89(1H,m), 6.51(1H,s), 7.00-7.09(2H,m), 7.22-7.35(5H,m), 7.49(2H,d,J=8.4Hz), 8.84(1H,brs)
119	NMR ($CDCl_3$) δ: 1.40(9H,s), 2.28-2.75(2H,m), 3.10-3.64(6H,m), 4.81(1H,brs), 6.34(1H,brs), 6.98(2H,d,J=8.1Hz), 7.18-7.42(7H,m), 8.76(1H,brs)
120	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.10-3.50(4H,m), 3.69(2H,s), 4.30(1H,brs), 4.87-4.88(1H,m), 6.44(1H,m), 7.00-7.50(13H,m), 9.11(1H,s)
121	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.50-2.80(2H,m), 3.10-3.50(4H,m), 3.70(2H,s), 4.85-4.90(1H,m), 5.30(2H,s), 6.96-7.36(11H,m), 7.41(2H,d,J=8.3Hz), 8.18(2H,d,J=8.3Hz)
122	NMR ($CDCl_3$) δ: 2.20-3.50(6H,m), 3.63(2H,s), 4.87-4.88(1H,m), 5.54(1H,brs), 6.38(1H,s), 7.26-7.45(9H,m), 8.93(1H,brs)
123	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.60-3.60(6H,m), 4.87-4.91(1H,m), 5.03(2H,brs), 7.02-7.38(7H,m), 7.46(1H,s), 7.55-7.60(2H,m), 8.93(1H,brs)
124	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.25(3H,s), 2.60-3.50(6H,m), 3.52(2H,s), 4.83(1H,s), 7.27-7.45(9H,m), 9.01(1H,brs)
125	NMR ($CDCl_3$) δ: 1.47(9H,s), 1.59(6H,s), 2.55-3.60(6H,m), 5.01(1H,s), 6.34(1H,s), 6.95-7.50(9H,m), 9.25(1H,brs)
126	NMR ($CDCl_3$) δ: 1.47(9H,s), 1.75-3.80(13H,m), 4.86(1H,brs), 6.99-7.50(9H,m)

[0133]

[Table 8]

Rex.	D A T A
127	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.55-2.75(2H,m), 3.15-3.55(4H,m), 3.75(2H,s), 4.33(1H,brs), 4.87(1H,br), 6.86(1H,d,J=4.4Hz), 6.97-7.15(2H,m), 7.23-7.48 (9H,m), 9.28(1H,brs)
128	NMR ($CDCl_3$) δ: 1.43(9H,s), 2.55-3.50(6H,m), 3.78(2H,s), 4.89(1H,brs), 5.41(2H,s), 6.98-7.44(14H,m), 7.86(1H,s), 9.87(1H,brs)
129	NMR ($CDCl_3$) δ: 1.45(9H,s), 2.55-3.51(6H,m), 3.85(2H,s), 4.87(1H,brs), 5.29(2H,s), 7.04(2H,brs), 7.22-7.43(12H,m), 8.02(1H,s), 9.27(1H,brs)
130	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.60-3.40(6H,m), 3.50(2H,s), 4.79-4.85(1H,m), 5.63(2H,s), 6.57(1H,s), 7.01-7.46(14H,m)
131	NMR ($CDCl_3$) δ: 1.46(9H,s), 1.77-1.98(3H,m), 2.56-2.88(5H,m), 3.10-3.55(4H,m), 3.82-3.90(1H,m), 4.35(1H,brs), 4.80-4.93(1H,m), 6.97-7.10(2H,m), 7.15(1H,dd,J=7.6, 4.8Hz), 7.24-7.37(5H,m), 7.43-7.48(3H,m), 8.45(1H,dd,J=4.4, 1.6Hz), 10.01(1H,brs)
132	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.52-2.80(2H,m), 3.20-3.52(4H,m), 3.73(2H,s), 4.88(1H,brs), 7.00-7.40(11H,m), 7.45-7.51(5H,m), 10.41(1H,brs)
133	NMR ($CDCl_3$) δ: 1.22(6H,d,J=6.9Hz), 1.47(9H,s), 2.50-3.50(7H,m), 3.89(2H,s), 4.85-4.94(1H,m), 5.27(2H,s), 6.91(1H,s), 7.00-7.45(10H,m), 7.57(2H,d,J=8.3Hz), 10.12(1H,brs)
134	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.50-2.80(2H,m), 3.20-3.60(6H,m), 4.30(1H,brs), 4.88(1H,brs), 4.99(2H,s), 6.70(1H,s), 6.97-7.52(28H,m)
135	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.69(2H,brs), 3.11-3.43(4H,m), 3.74(2H,s), 4.37(1H,brs), 4.88(1H,brs), 5.22(2H,s), 6.72(1H,brd,J=7.2Hz), 6.91(1H,d,J=4.5Hz), 7.05(2H,brs), 7.10(1H,d,J=4.5Hz), 7.16-7.35(7H,m), 7.42(1H,d,J=8.1Hz), 7.48(2H,d,J=8.4Hz), 10.40(1H,brs)
136	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.69(2H,brs), 3.20-3.50(4H,m), 3.71(2H,s), 4.81(1H,brs), 4.88(1H,brs), 5.14(2H,s), 6.93(2H,brs), 7.06(3H,brd,J=8.4Hz), 7.26-7.35(8H,m), 7.45(2H,d,J=8.4Hz), 10.20(1H,brs)
137	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.70(2H,brs), 3.15-3.40(4H,m), 3.71(2H,s), 4.88(1H,brs), 5.13(2H,s), 6.72(1H,brd,J=7.2Hz), 6.90-7.44(14H,m), 10.01(1H,brs)
138	NMR ($CDCl_3$) δ: 1.46(9H,s), 2.70(2H,brs), 3.36(4H,brs), 4.40(2H,s), 4.89(1H,brs), 5.58(2H,s), 7.03-7.37(10H,m), 7.55-7.77(5H,m), 10.19(1H,brs)
139	NMR ($CDCl_3$) δ: 1.46(9H,s), 1.55(9H,s), 2.55-2.85(2H,m), 3.15-3.55(4H,m), 3.76(2H,s), 4.86(1H,dd,J=8.0, 3.2Hz), 6.94-7.15(3H,m), 7.21-7.48(6H,m), 7.63-7.84(3H,m), 9.03(1H,brs)
140	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.55-2.85(2H,m), 3.12-3.54(4H,m), 3.67(2H,s), 4.56(2H,brs), 4.81-4.92(1H,m), 6.42(1H,d,J=8.4Hz), 6.63(1H,d,J=7.2Hz), 6.97-7.15(2H,m), 7.21-7.46(8H,m), 9.66(1H,brs)
141	NMR ($CDCl_3$) δ: 0.97(6H,d,J=6.3Hz), 1.46(9H,s), 2.06-2.17(1H,m), 2.50-3.50(6H,m), 4.00(2H,d,J=7.8Hz), 4.11(2H,s), 4.83-4.92(1H,m), 6.95(1H,d,J=1.5Hz), 7.00-7.10(2H,m), 7.14(1H,d,J=1.5Hz), 7.22-7.40(9H,m), 7.59(2H,d,J=8.0Hz), 10.11(1H,brs)

[0134]

[Table 9]

Rex.	D A T A
142	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.15-3.55(4H,m), 3.78(2H,s), 4.36(1H,brs), 4.82-4.94(1H,m), 5.18(2H,s), 6.92-6.99(2H,m), 7.00-7.13(5H,m), 7.25-7.38(6H,m), 7.42-7.48(2H,m), 10.34(1H,brs)
143	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.10-3.55(4H,m), 3.70(2H,s), 4.40(1H,brs), 4.87-4.89(1H,m), 5.16(2H,s), 6.75(1H,d,J=10.2Hz), 6.86(1H,d,J=8.3Hz), 6.90-7.40(11H,m), 7.45(2H,d,J=8.3Hz), 10.22(1H,brs)
144	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.77(2H,m), 3.20-3.54(4H,m), 3.78(2H,s), 4.33-4.42(1H,m), 4.84-4.94(1H,m), 5.14(2H,s), 6.80-7.10(8H,m), 7.31-7.37(4H,m), 7.46(2H,d,J=8.3Hz), 10.19(1H,s)
145	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.70(2H,brs), 3.35(4H,brs), 3.92(2H,s), 4.36(1H,brs), 4.89(1H,brs), 5.17(2H,s), 6.92-7.07(6H,m), 7.26-7.35(6H,m), 7.48(2H,d,J=8.7Hz), 10.29(1H,brs)
146	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.15-3.55(4H,m), 3.69(2H,s), 4.35(1H,brs), 4.83-4.94(1H,m), 5.15(2H,s), 6.53-6.62(2H,m), 6.75(1H,tt,J=8.8, 2.0Hz), 6.94(1H,s), 7.00-7.15(3H,m), 7.25-7.39(5H,m), 7.42-7.48(2H,m), 10.09(1H,brs)
147	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.70(2H,brs), 3.36(4H,brs), 3.77(2H,s), 4.87(1H,brs), 5.17(2H,s), 6.60(1H,m), 6.95(1H,s), 6.95-7.09(5H,m), 7.25-7.35(5H,m), 7.46(2H,d,J=8.4Hz), 10.21(1H,brs)
148	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.70(2H,m), 3.10-3.60(4H,m), 3.70(2H,s), 4.85-4.90(1H,m), 5.12(2H,s), 6.80-6.95(3H,m), 7.00-7.20(4H,m), 7.50-7.90(5H,m), 7.44(2H,d,J=8.4Hz), 10.05(1H,brs)
149	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.10-4.05(4H,m), 3.92(2H,s), 4.35(1H,brs), 4.85-4.94(1H,m), 5.20(2H,s), 6.90-7.25(7H,m), 7.30-7.40(4H,m), 7.48(2H,d,J=8.4Hz), 10.25(1H,brs)
150	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.15-3.55(4H,m), 3.77(2H,s), 4.37(1H,brs), 4.82-4.94(1H,m), 5.15(2H,s), 6.74-6.82(1H,m), 6.90-7.14(5H,m), 7.24-7.37(5H,m), 7.42-7.48(2H,m), 10.04(1H,brs)
151	NMR ($CDCl_3$) δ: 1.51(9H,s), 2.60-2.75(2H,m), 3.10-3.65(4H,m), 3.70(2H,s), 4.36(1H,brs), 4.85-4.93(1H,m), 5.12(2H,s), 6.69(2H,t,J=6.8Hz), 6.92(1H,s), 7.00-7.15(3H,m), 7.25-7.40(5H,m), 7.43(2H,d,J=8.3Hz), 9.91(1H,brs)
152	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.77(2H,m), 3.20-3.50(4H,m), 3.90(2H,s), 4.33-4.42(1H,m), 4.84-4.92(1H,m), 5.25(2H,s), 6.93(1H,s), 7.00-7.08(2H,m), 7.30-7.37(5H,m), 7.46(2H,d,J=8.3Hz), 10.03(1H,s)
153	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.15-3.55(4H,m), 3.71(2H,s), 4.38(1H,brs), 4.82-4.94(1H,m), 5.10(2H,s), 6.93(1H,s), 6.99-7.11(5H,m), 7.23-7.48(8H,m), 7.62-7.67(2H,m), 10.18(1H,brs)
154	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.69(2H,brs), 3.36(4H,brs), 3.98(2H,s), 4.41(1H,brs), 4.89(1H,brs), 5.35(2H,s), 6.68(1H,d,J=1.5Hz), 7.00(1H,d,J=1.5Hz), 7.07(2H,m), 7.26-7.41(8H,m), 7.49(2H,d,J=8.4Hz), 10.29(1H,brs)
155	NMR ($CDCl_3$) δ: 1.47(9H,s), 2.70(2H,brs), 3.36(4H,brs), 3.69(2H,s), 4.89(1H,brs), 5.27(2H,s), 6.92(1H,brd,J=1.2Hz), 7.05-7.35(10H,m), 7.40(2H,d,J=8.4Hz), 7.61(2H,d,J=8.1Hz), 9.93(1H,brs)

[0135]

[Table 10]

Rex.	D A T A
156	NMR (CDCl3) δ: 1.47(9H,s), 2.69(2H,brs), 3.36(4H,brs), 3.84(2H,s), 4.43(1H,brs), 4.88(1H,brs), 5.43(2H,s), 7.04-7.06(4H,m), 7.11(1H,d,J=1.2Hz), 7.26-7.35(5H,m), 7.45(2H,d,J=8.4Hz), 7.55(1H,t,J=6.9Hz), 7.69-7.74(1H,m), 7.79(1H,d,J=8.1Hz), 8.01(1H,d,J=8.6Hz), 8.11(1H,d,J=8.6Hz), 10.36(1H,brs)
157	NMR (CDCl3) δ: 1.47(9H,s), 2.70(2H,brs), 3.36(4H,brs), 3.96(2H,s), 4.40(1H,brs), 4.89(1H,brs), 5.25(2H,d,J=1.5Hz), 6.87(1H,s), 6.99(1H,s), 7.03-7.10(3H,m), 7.25-7.35(7H,m), 7.49(2H,d,J=8.4Hz), 10.28(1H,brs)
158	NMR (CDCl3) δ: 1.47(9H,s), 2.70(2H,brs), 3.36(4H,brs), 3.74(2H,s), 4.42(1H,brs), 4.88(1H,brs), 5.19(2H,s), 6.74(1H,dd,J=8.4, 8.0Hz), 6.89-6.94(2H,m), 7.09-7.35(9H,m), 7.46(2H,d,J=8.4Hz), 10.26(1H,brs)
159	NMR (CDCl3) δ: 1.47(9H,s), 2.60-2.77(2H,m), 3.20-3.60(4H,m), 3.73(2H,s), 4.30-4.40(1H,m), 4.84-4.94(1H,m), 5.20(2H,s), 6.66(1H,d,J=2.5Hz), 6.92(1H,s), 7.00-7.20(3H,m), 7.22-7.52(9H,m), 10.25(1H,s)
160	NMR (CDCl3) δ: 1.47(9H,s), 2.60-2.75(2H,m), 3.25-3.55(4H,m), 3.77(2H,s), 4.30-4.40(1H,m), 4.84-4.92(1H,m), 5.18(2H,s), 6.67-6.75(1H,m), 6.88-6.96(2H,m), 7.02-7.12(3H,m), 7.31-7.36(5H,m), 7.45(2H,d,J=8.3Hz), 10.06(1H,s)
161	NMR (CDCl3) δ: 1.47(9H,s), 2.60-2.80(2H,m), 3.20-3.60(4H,m), 3.70(2H,s), 3.91(3H,s), 4.82-4.95(1H,m), 5.23(2H,s), 6.94(1H,s), 6.99-7.50(13H,m), 7.94-8.03(2H,m), 10.18(1H,brs)
162	NMR (CDCl3) δ: 1.47(9H,s), 1.60-1.70(6H,m), 2.60-2.80(2H,m), 3.20-3.40(5H,m), 3.60-3.75(3H,m), 3.71(2H,s), 4.30-4.40(1H,m), 4.80-4.90(1H,m), 5.17(2H,s), 6.95(1H,s), 7.00-7.20(5H,m), 7.30-7.50(10H,m), 10.28(1H,s)
163	NMR (CDCl3) δ: 1.47(9H,s), 2.60-2.90(2H,m), 3.16-3.56(4H,m), 4.01(2H,s), 4.20-4.30(1H,m), 4.80-4.95(1H,m), 7.00-7.20(2H,m), 7.25-7.38(5H,m), 7.44(2H,d,J=8.4Hz), 8.07(1H,s)
164	NMR (CDCl3) δ: 1.47(9H,s), 2.60-2.88(2H,m), 3.10-3.54(4H,m), 4.20-4.35(1H,m), 4.85-4.90(1H,m), 4.93(2H,s), 6.38-6.40(1H,m), 7.00-7.15(2H,m), 7.30-7.40(7H,m), 7.53(1H,d,J=2.0Hz), 7.71(1H,d,J=2.0Hz), 8.34(1H,s)
165	NMR (CDCl3) δ: 1.46(9H,s), 2.60-2.84(2H,m), 3.10-3.50(4H,m), 4.14-4.28(1H,m), 4.84-4.92(1H,m), 5.00(2H,s), 7.02-7.10(2H,m), 7.30-7.40(7H,m), 8.12(1H,s), 8.24(2H,s)
166	NMR (CDCl3) δ: 1.43(9H,s), 2.60-2.80(2H,m), 3.10-3.50(4H,m), 4.64(2H,s), 4.75-4.85(1H,m), 6.90-7.00(4H,m), 7.20-7.35(9H,m), 8.50-8.80(1H,m)
167	NMR (CDCl3) δ: 2.62-3.00(6H,m), 3.50-3.65(2H,m), 3.95(1H,d,J=13.2Hz), 4.67(1H,dd,J=10.4, 4.0Hz), 7.18-7.40(12H,m), 8.05-8.15(2H,m)
168	NMR (CDCl3) δ: 2.56-2.94(6H,m), 3.40-3.65(2H,m), 3.80(1H,brs), 3.95(1H,d,13.6Hz), 4.62(1H,dd,J=10.0, 3.2Hz), 6.57-6.66(2H,m), 6.87-6.98(2H,m), 7.20-7.37(10H,m)
169	NMR (CDCl3) δ: 2.54-2.98(6H,m), 3.50-4.02(5H,m), 4.62(1H,dd,J=10.0, 3.6Hz), 6.80-7.70(17H,m), 8.60(1H,d,J=5.6Hz), 9.73(1H,br)

[0136]

[Table 11]

Rex.	D A T A
170	NMR ($CDCl_3$) δ: 2.54-2.98(6H,m), 3.50-3.74(3H,m), 3.96(1H,d,J=13.6Hz), 4.59(1H,dd,J=10.0, 3.6Hz), 7.00-7.80(16H,m), 8.50-8.62(2H,m)
171	NMR ($CDCl_3$) δ: 2.54-3.02(6H,m), 3.50-3.75(3H,m), 3.96(1H,d,J=13.6Hz), 4.59(1H,dd,J=10.4, 4.0Hz), 7.00-7.60(16H,m), 8.55-8.65(2H,m)
172	NMR ($CDCl_3$) δ: 2.54-3.02(6H,m), 3.50-4.04(3H,m), 3.65(1H,d,J=13.6Hz), 4.59(1H,dd,J=10.0, 4.0Hz), 7.00-8.00(19H,m), 8.61(1H,d,J=4.4Hz)
173	NMR ($CDCl_3$) δ: 1.22(6H,d,J=6.9Hz), 1.47(9H,s), 2.50-3.50(7H,m), 3.89(2H,s), 4.85-4.94(1H,m), 5.27(2H,s), 6.91(1H,s), 7.00-7.45(10H,m), 7.57(2H,d,J=8.3Hz), 10.12(1H,brs)
174	NMR ($CDCl_3$) δ: 2.57-2.96(3H,m), 3.58(1H,d,J=14.0Hz), 3.97(1H,d,J=4.0Hz), 4.04(2H,d,J=1.2Hz), 4.58(1H,dd,J=10.0, 3.2Hz), 7.10(2H,d,J=8.4Hz), 7.21-7.33(14H,m), 7.50(2H,d,J=8.4Hz), 9.82(1H,brs)
175	NMR ($CDCl_3$) δ: 2.40(3H,s), 2.54-3.00(6H,m), 3.57(1H,d,J=13.6Hz), 3.88(2H,s), 3.95(1H,d,J=13.6Hz), 4.62(1H,dd,J=10.4, 3.6Hz), 7.00-7.75(16H,m), 8.44(1H,d,J=4.4Hz), 9.66(1H,brs)
176	NMR ($CDCl_3$) δ: 2.54-3.00(6H,m), 3.57(1H,d,J=13.6Hz), 3.89(2H,s), 3.95(1H,d,J=13.6Hz), 4.61(1H,dd,J=10.0, 3.6Hz), 7.00-7.50(14H,m), 8.45-8.70(3H,m), 8.91(1H,brs)
177	NMR ($CDCl_3$) δ: 2.59-2.94(6H,m), 3.57(1H,d,J=14.6Hz), 3.72(2H,s), 3.96(1H,d,J=14.6Hz), 4.63(1H,dd,J=10.4, 4.0Hz), 5.14(2H,s), 6.90(1H,s), 7.04-7.10(4H,m), 7.24-7.36(14H,m), 7.46(2H,d,J=8.4Hz), 10.27(1H,s)
178	NMR ($CDCl_3$) δ: 2.31(3H,s), 2.89-3.19(6H,m), 3.98(2H,s), 3.72(2H,s), 4.96(1H,dt,J=3.2, 10.4Hz), 7.03-7.40(17H,m), 10.30(1H,s)
179	NMR ($CDCl_3$) δ: 2.24(3H,s), 2.82-3.20(6H,m), 3.81(2H,s), 3.99(2H,s), 5.01(1H,dt,J=10.0, 3.6Hz), 7.14-7.61(17H,m), 10.36(1H,s)
180	NMR ($CDCl_3$) δ: 2.42(3H,s), 2.70-3.19(6H,m), 3.69(2H,s), 3.93(2H,s), 4.94(1H,dt,J=3.2, 10.0Hz), 7.05-7.69(17H,m), 10.26(1H,s)
181	NMR ($CDCl_3$) δ: 1.10(3H,d,J=6.4Hz), 2.73(1H,dd,J=13.2, 6.4Hz), 2.89(1H,dd,J=13.2, 6.8 Hz), 2.95-3.06(1H,m), 3.76 (1H,d,J=13.2Hz), 3.86(1H,d,J=13.2Hz), 7.16-7.40(7H,m), 8.01-8.22(2H,m)
182a	NMR ($CDCl_3$) δ: 1.07(3H,d,J=6.4Hz), 2.50-2.75(3H,m), 2.88(1H,dd,J=13.6, 8.8Hz), 3.15-3.30(1H,m), 3.51(1H,d,J=13.2Hz), 3.88(1H,d,J=13.2Hz), 4.62(1H,dd,J=10.4, 4.0Hz), 6.80-7.60(12H,m), 8.00-8.15(2H,m)
182b	NMR ($CDCl_3$) δ: 1.05(3H,d,J=6.4Hz), 2.47(1H,dd,J=14.4, 10.4Hz), 2.62-2.85(2H,m), 3.03-3.18(2H,m), 3.62(1H,brs), 3.75(1H,d,J=13.2Hz), 3.89(1H,d,J=13.2Hz), 4.51(1H,dd,J=9.6, 3.2Hz), 7.14-7.44(12H,m), 8.05-8.20(2H,m)
183	NMR ($CDCl_3$) δ: 1.00(3H,d,J=6.8Hz), 2.45-2.77(4H,m), 3.13-3.18(1H,m), 3.40-3.78(4H,m), 3.91(1H,d,J=13.6Hz), 4.56(1H,dd,J=10.4, 3.6Hz), 6.55-6.68(2H,m), 6.80-6.93(2H,m), 7.13-7.40(10H,m)
184	NMR ($CDCl_3$) δ: 1.04(3H,d,J=6.8Hz), 2.27(1H,dd,J=13.2, 9.6Hz), 2.62(1H,dd,J=13.2, 10.4Hz), 2.75(1H,dd,J=13.2, 4.0Hz), 3.30-4.10(5H,m), 4.42(1H,dd,J=10.0, 4.0Hz), 6.55-6.68(2H,m), 6.83-6.95(2H,m), 7.20-7.40(10H,m)

[0137]

[Table 12]

Rex.	D A T A
185	NMR (CDCl3) δ: 1.00(3H,d,J=6.8Hz), 2.54-2.65(3H,m), 2.70-2.82(1H,m), 3.08-3.20(1H,m), 3.44-3.98(5H,m), 4.55(1H,dd,J=10.4, 3.6Hz), 6.80-7.60(16H,m), 7.64-7.74(1H,m), 8.50-8.70(1H,m), 9.72(1H,brs)
186	NMR (CDCl3) δ: 1.02(3H,d,J=6.8Hz), 2.32(1H,dd,J=12.8, 8.8Hz), 2.63(1H,dd,J=13.2, 10.4Hz), 2.75(1H,dd,J=13.2, 3.6Hz), 2.95-3.10(2H,m), 3.70-3.92(4H,m), 4.44(1H,dd,J=9.6, 3.6Hz), 7.00-7.06(2H,m), 7.16-7.38(11H,m), 7.62-7.72(2H,m), 8.61(1H,d,J=4.4Hz), 9.74(1H,brs)
187	NMR (CDCl3) δ: 1.03(3H,d,J=6.8Hz), 2.32(1H,dd,J=13.2, 9.2Hz), 2.64(1H,dd,J=13.2, 10.4Hz), 2.75(1H,dd,J=13.2, 3.6Hz), 2.95-3.10(2H,m), 3.65-3.93(4H,m), 4.45(1H,dd,J=10.4, 4.0Hz), 5.14(2H,s), 6.92-7.50(21H,m), 10.30(1H,brs)
188	NMR (CDCl3) δ: 2.58-2.65(1H,m), 2.75-3.00(5H,m), 3.59(1H,d,J=13.2Hz), 3.95(1H,d,J=13.2Hz), 5.01(1H,dd,J=10.0, 3.2Hz), 6.97-7.03(1H,m), 7.12-7.35(9H,m), 7.48-7.56(1H,m), 8.04-8.13(2H,m)
189	NMR (CDCl3) δ: 2.65(1H,d,J=10.0, 12.4Hz), 2.72-3.00(5H,m), 3.57(1H,d,J=13.2Hz), 3.94(1H,d,J=13.2Hz), 4.64(1H,dd,J=10.0, 3.2Hz), 6.92-7.08(3H,m), 7.20-7.36(8H,m), 8.11(2H,d,J=8.8Hz)
190	NMR (CDCl3) δ: 2.57-3.00(6H,m), 3.56(1H,d,J=13.2Hz), 3.95(1H,d,J=13.2Hz), 4.63(1H,dd,J=10.0, 3.2Hz), 6.99-7.04(2H,m), 7.21-7.35(9H,m), 8.12(2H,d,J=8.4Hz)
191	NMR (CDCl3) δ: 2.52-2.59(1H,m), 2.64-2.93(5H,m), 3.58(1H,d,J=13.6Hz), 3.72-3.76(1H,m), 3.96(1H,d,J=13.6Hz), 4.98(1H,dd,J=2.8, 10.4Hz), 6.60-6.64(2H,m), 6.61-7.35(10H,m), 7.47-7.59(1H,m)
192	NMR (CDCl3) δ: 2.51-2.59(1H,m), 2.64-2.90(5H,m), 3.57(1H,d,J=13.2Hz), 3.94(1H,d,J=13.2Hz), 4.59(1H,dd,J=10.0, 3.2Hz), 6.60-6.64(2H,m), 6.90-6.94(3H,m), 7.00-7.05(2H,m), 7.23-7.35(6H,m)
193	NMR (CDCl3) δ: 2.52-2.92(6H,m), 3.57(1H,d,J=13.6Hz), 3.80(1H,s), 3.96(1H,d,J=13.6Hz), 4.58(1H,dd,J=10.2, 3.6Hz), 6.60-6.64(2H,m), 6.91-7.02(4H,m), 7.22-7.35(7H,m)
194	NMR (CDCl3) δ: 2.53-2.60(1H,m), 2.68-2.94(5H,m), 3.58(1H,d,J=13.2Hz), 3.86(2H,s), 3.95(1H,d,J=13.2Hz), 4.97(1H,dd,J=2.8, 10.0Hz), 6.94-7.35(12H,m), 7.44-7.51(3H,m), 7.67-7.72(1H,m), 8.60-8.63(1H,m), 9.72(1H,s)
195	NMR (CDCl3) δ: 2.52-2.59(1H,m), 2.66-2.94(5H,m), 3.57(1H,d,J=13.2Hz), 3.86(2H,s), 3.94(1H,d,J=13.2Hz), 4.58(1H,dd,J=10.4, 3.6Hz), 6.89-7.07(4H,m), 7.19-7.35(9H,m), 7.45-7.48(2H,m), 7.62-7.72(1H,m), 8.60-8.64(1H,m), 9.74(1H,s)
196	NMR (CDCl3) δ: 2.52-2.94(6H,m), 3.56(1H,d,J=13.2Hz), 3.86(2H,s), 3.94(1H,d,J=13.2Hz), 4.57(1H,dd,J=10.0, 3.2Hz), 6.96-7.08(4H,m), 7.21-7.35(9H,m), 7.45-7.48(2H,m), 7.66-7.72(1H,m), 8.60-8.64(1H,m), 9.73(1H,s)
197	NMR (CDCl3) δ: 3.70(2H,s), 3.88(2H,s), 7.23-7.32(4H,m), 7.54-7.62(2H,m), 7.71(1H,dt,J=7.6, 1.6Hz), 8.63(1H,d), 10.04(1H,brs)

[0138]

[Table 13]

Rex.	D A T A
198	NMR (CDCl3) δ: 3.72(2H,s), 4.13(2H,s), 7.26-7.31(3H,m), 7.58-7.63(2H,m), 8.78(2H,d,J=5.2Hz), 9.82(1H,brs)
199	NMR (CDCl3) δ: δ :3.71(2H,s), 4.08(2H,s), 7.25-7.30(2H,m), 7.40(1H,d,J=8.4Hz), 7.57-7.66(3H,m), 7.77-7.89(2H,m), 8.12(1H,d,J=8.4Hz), 8.20(1H,d,J=8.4Hz), 10.60(1H,brs)
200	NMR (CDCl3) δ: 2.31(3H,s), 2.59(3H,s), 3.71(2H,s), 3.77(2H,s), 6.91(1H,s), 6.93(1H,s), 7.24-7.28(2H,m), 7.55-7.60(2H,m), 10.60(1H,brs)
201	NMR (CDCl3) δ: 3.70(2H,s), 3.97(2H,s), 5.42(2H,s), 3.74(2H,s), 7.01(1H,d,J=8.5Hz), 6.89-6.94(2H,m), 7.22-7.37(7H,m), 7.56(2H,d,J=8.5Hz), 7.78-7.81(1H,m), 10.68(1H,brs)
202	NMR (CDCl3) δ: 2.26(3H,s), 2.39(3H,s), 2.57(2H,t,J=7.2Hz), 2.72(2H,t,J=7.2Hz), 3.72(2H,s), 6.95(1H,s), 7.01(1H,s), 7.11(2H,d,J=8.8Hz), 7.51(2H,d,J=8.8Hz), 10.17(1H,s)
203	NMR δ: 2.32(3H,s), 2.41(3H,s), 2.90-3.19(6H,m), 3.75(2H,s), 4.01(2H,s), 4.89(1H,dt,J=7.6, 3.2Hz), 6.99-7.71(16H,m), 10.26(1H,s)
204	NMR (CDCl3) δ: 1.47(9H,s), 1.70-1.82(2H,m), 2.59(2H,t,d,J=8.0Hz), 3.04-3.20(2H,m), 3.86(2H,s), 4.52(1H,brs), 7.05-7.15(2H,m), 7.20-7.33(2H,m), 7.40-7.50(2H,m), 7.69(1H,dt,J=2.0, 8.0Hz), 8.55-8.65(1H,m), 9.70(1H,brs)
205	NMR (CDCl3) δ: 1.45(9H,s), 3.42-3.60(2H,m), 3.86(2H,s), 3.98(2H,t,J=5.2Hz), 5.00(1H,brs), 6.77-6.88(2H,m), 7.21-7.28(1H,m), 7.22(1H,d,J=8.0Hz), 7.40-7.50(2H,m), 7.70(1H,dt,J=8.0, 2.0Hz), 8.57-8.65(1H,m), 9.68(1H,brs)
206	NMR (CDCl3) δ: 1.24(6H,s), 1.46(9H,s), 2.93(2H,s), 3.87(2H,s), 4.24(1H,brs), 7.05-7.13(2H,m), 7.18-7.33(2H,m), 7.42-7.50(2H,m), 7.66-7.73(1H,m), 8.58-8.66(1H,m), 9.73(1H,brs)
207	NMR (CDCl3) δ: 1.65-1.85(2H,m), 2.55-2.64(2H,m), 2.66-2.74(2H,m), 3.86(2H,s), 7.07-7.15(2H,m), 7.20-7.35(4H,m), 7.40-7.50(2H,m), 7.65-7.73(1H,m), 8.54-8.64(1H,m), 9.70(1H,brs)
208	NMR (CDCl3) δ: 1.48(9H,s), 2.60-2.85(2H,m), 3.15-3.60(4H,m), 4.30-4.40(1H,m), 4.80-4.95(1H,m), 6.77(1H,d,J=8.3Hz), 6.92-6.97(1H,m), 7.05-7.15(2H,m), 7.31-7.36(4H,m), 7.51(2H,d,J=8.3Hz), 7.60-7.68(2H,m), 8.26(1H,dt,J=4.9, 1.0Hz), 11.71(1H,s)

[0139]

[Table 14]

Ex.	DATA
1	mp : 223-225°C NMR δ: 2.95-3.28(6H,m), 4.98-5.07(1H,m), 7.23-7.44(6H,m), 7.65-7.75(1H,m), 7.88(2H,d,J=8.4Hz), 8.05-8.22(2H,m), 8.75(1H,d,J=4.4Hz), 8.97(1H,brs), 9.43(1H,brs), 10.65(1H,brs)
2	mp : 263-265°C NMR δ: 2.92-3.10(3H,m), 3.13-3.27(3H,m), 5.00(1H,dd,J=10.8, 2.8Hz), 7.24-7.44(8H,m), 7.74-7.81(3H,m), 8.57(1H,d,J=8.0Hz), 8.81-8.96(2H,m), 9.20-9.30(2H,m), 10.71(1H,brs)
3	mp : 145-147°C NMR δ: 2.94-3.10(3H,m), 3.14-3.30(3H,m), 4.97-5.05(1H,m), 7.27-7.46(7H,m), 7.77-7.90(4H,m), 8.30(1H,dd,J=8.4, 1.6Hz), 8.60-8.71(2H,m), 8.89(1H,brs), 9.10-9.30(2H,m), 13.12(1H,brs)
4	mp : 246-248°C (dec) NMR δ: 2.92-3.09(3H, m), 3.11-3.26(3H,m), 5.01(1H,dd,J=10.4, 2.8Hz), 7.24(2H,d,J=8.4Hz), 7.29-7.47(6H,m), 7.56-7.75(4H,m), 7.85(1H,d,J=8.0Hz), 8.11(1H,t,J=7.6Hz), 8.73(1H,d,J=4.4Hz), 8.92(1H,brs), 9.32(1H,brs), 10.69(1H,brs)
5	mp : 228-233°C (dec) NMR δ: 2.88-3.09(3H,m), 3.10-3.24(3H,m), 4.30(2H,s), 4.93-5.01(1H,m), 6.19(1H,d,J=3.6Hz), 7.18-7.27(2H,m), 7.28-7.53(7H,m), 7.57-7.62(2H,m), 7.97(1H,d,J=7.6Hz), 8.08(1H,d,J=8.0Hz), 8.83(1H,brs), 9.11(1H,brs), 10.57(1H,brs)
6	mp : 161-162°C NMR δ: 2.86-3.24(6H,m), 4.24(2H,s), 4.97(1H,dd,J=9.6, 2.8Hz), 7.16-7.23(2H,m), 7.27-7.44(5H,m), 7.55(1H,s), 7.61(2H,d,J=8.4Hz), 7.85(1H,s), 8.27(1H,d,J=2.4Hz), 8.97(1H,brs), 9.47(1H,brs), 10.94(1H,brs)
7	MS (m/z) : 396[$(M+H)^+$] NMR δ: 2.70(3H,s), 2.86-3.27(6H,m), 3,85(2H,s), 5.00-5.05(1H,m), 7.18-7.60(10H,m), 10.43(1H,s)
8	mp : 203-207°C NMR δ: 2.92-3.08(3H,m), 3.10-3.22(3H,m), 4.28(2H,s), 5.01(1H,d,J=7.8Hz), 6.21(1H,brs), 7.22(2H,d,J=8.3Hz), 7.25-7.63(4H,m), 8.93(1H,brs), 9.38(1H,brs), 10.86(1H,s)
9	mp : 259-261°C NMR δ: 2.90-3.10(3H,m), 3.10-3.25(3H,m), 4.15(2H,s), 4.97(1H,d,J=10.8Hz), 6.20(1H,d,J=3.9Hz), 7.21(2H,d,J=8.8Hz), 7.30-7.42(5H,m), 7.57(2H,d,J=8.8Hz), 8.85(1H,brs), 9.14(1H,brs), 10.58(1H,s)
10	mp : 210-213°C NMR δ: 2.86-3.08(3H,m), 3.12-3.22(3H,m), 3.73(2H,s), 4.91-4.98(1H,m), 6.19(1H,d,J=3.9Hz), 7.21(2H,d,J=8.3Hz), 7.29-7.42(5H,m), 7.54(2H,d,J=8.3Hz), 8.78(1H,brs), 8.99(1H,brs), 10.35(1H,s), 13.21(1H,brs), 13.34(1H,brs)

[0140]

[Table 15]

Ex.	D A T A
11	mp : 205-210°C (dec) NMR δ: 2.90-3.25(6H,m), 4.95-5.04(1H,m), 7.23-7.44(7H,m), 7.67-7.75(2H,m), 8.15(1H,s), 8.88(1H,brs), 9.25(1H,brs), 10.83(1H,brs)
12	mp : 244-246°C NMR δ: 2.90-3.08(3H,m), 3.10-3.20(3H,m), 3.67(2H,s), 5.00(1H,dd,J=2.4,10.02Hz), 7.19(2H,d,J=8.3Hz), 7.28-7.42(5H,m), 7.57(2H,d,J=8.3Hz), 8.90(1H,s), 9.31(1H,s), 10.31(1H,s)
13	mp : 205-208°C NMR δ: 1.27(3H,t,J=7.1Hz), 2.88-3.08(3H,m), 3.12-3.22(3H,m), 3.86(2H,s), 4.27(2H,q,J=7.1Hz), 4.96(1H,d,J=8.3Hz), 6.20(1H,s), 7.19(2H,d,J=8.3Hz), 7.30-7.42(5H,m), 7.57(2H,d,J=8.3Hz), 8.81(1H,s), 9.10(1H,s), 10.33(1H,s), 12.53(1H,s)
14	mp : 169-173°C NMR δ: 2.88-3.22(6H,m), 3.66(2H,s), 4.98(1H,dd,J=2.9, 13.1Hz), 6.72(1H,s), 7.19(2H,d,J=8.3Hz), 7.23-7.42(8H,m), 7.59(2H,d,J=8.3Hz), 7.72-7.78(1H,m), 8.85(1H,s), 9.18(1H,brs), 10.24(1H,brs), 10.55(1H,s)
15	mp : 248-251°C NMR δ: 2.90-3.08(3H,m), 3.09-3.21(3H,m), 3.88(2H,s), 5.02(1H,dd,J=10.0, 2.4Hz), 6.20(1H,brs), 7.16-7.22(2H,m), 7.28-7.46(7H,m), 7.57-7.63(2H,m), 7.84(1H,t,J=7.2Hz), 8.95(1H,brs), 9.40(1H,brs), 10.48(1H,brs)
16	mp : 237-238°C NMR δ: 2.87-3.24(6H,m), 3.77(2H,s), 4.93-5.03(1H,m), 5.32(2H,s), 6.20(1H,d,J=4.0Hz), 6.73(1H,d,J=8.0Hz), 6.99(1H,d,J=7.2Hz), 7.16-7.22(2H,m), 7.25-7.46(10H,m), 7.57-7.63(2H,s), 7.67(1H,dd,J=8.4, 7.2Hz), 8.87(1H,brs), 9.24(1H,brs), 10.30(1H,brs)
17	mp : 190-193°C NMR δ: 1.68(3H,m), 2.90-3.10(3H,m), 3.10-3.20(3H,m), 4.32(2H,s), 4.67(1H,s), 4.83(2H,s), 4.94(1H,s), 4.99(1H,d,J=8.3Hz), 6.21(1H,brs), 7.21(2H,d,J=8.7Hz), 7.24-7.42(5H,m), 7.56(2H,d,J=8.8Hz), 7.66(2H,d,J=1.9Hz), 7.71(1H,d,J=1.9Hz), 8.89(1H,brs), 9.30(1H,brs), 10.92(1H,s)
18	mp : 139-141°C NMR δ: 3.01(3H,brs), 3.15(3H,brs), 3.92(2H,s), 5.05(1H,d,J=10.3Hz), 5.44(2H,s), 6.19(1H,brs), 7.19(2H,d,J=8.3Hz), 7.31-7.47(10H,m), 7.60(2H,d,J=8.3Hz), 7.66(1H,s), 9.05(1H,brs), 9.35(1H,s), 9.60(1H,brs), 10.76(1H,s)
19	mp : 140-143°C NMR δ: 2.99-3.09(3H,m), 3.16(3H,brs), 3.95(2H,s), 5.06(1H,d,J=10.4Hz), 5.57(2H,s), 6.19(1H,brs), 7.19(2H,d,J=8.6Hz), 7.29-7.35(1H,m), 7.37-7.48(8H,m), 7.55-7.57(1H,m), 7.61(2H,d,J=8.6Hz), 9.09(1H,brs), 9.31(1H,d,J=1.5Hz), 9.65(1H,brs), 10.79(1H,s)

[0141]

[Table 16]

Ex.	DATA
20	mp : 140-143℃ NMR δ: 3.01-3.09(3H,m), 3.16(3H,brs), 3.93(2H,s), 5.06(1H,d,J=10.3Hz), 5.47(2H,s), 6.15(1H,brs), 7.19(2H,d,J=8.6Hz), 7.29-7.33(1H,m), 7.38-7.46(7H,m), 7.61(2H,d,J=8.6Hz), 7.63(1H,s), 7.70(1H,s), 9.08(1H,brs), 9.38(1H,s), 9.63(1H,brs), 10.78(1H,s)
21	mp : 141-146℃ NMR δ: 2.96-3.14(3H,m), 3.15(3H,brs), 3.91(2H,s), 5.04(1H,d,J=10.3Hz), 5.45(2H,s), 6.22(1H,brs), 7.19(2H,d,J=8.6Hz), 7.29-7.42(6H,m), 7.50(3H,s), 7.59(2H,d,J=8.6Hz), 7.65(1H,s), 9.02(1H,brs), 9.32(1H,d,J=1.5Hz), 9.55(1H,brs), 10.73(1H,s)
22	mp : 230-235℃ NMR δ: 2.59-3.10(3H,m), 3.10-3.25(3H,m), 4.47(2H,s), 5.01(1H,dd,J=10.3, 2.4Hz), 5.45(2H,s), 6.21(1H,brs), 7.16-7.22(4H,m), 7.28-7.50(7H,m), 7.54(2H,d,J=8.3Hz), 7.68(2H,dd,J=5.8, 1.9Hz), 8.94(1H,brs), 9.42(1H,brs), 10.98(1H,s)
23	mp : 203-209℃ NMR δ: 2.90-3.10(3H,m), 3.10-3.20(3H,m), 4.41-4.48(2H,m), 4.95-5.05(1H,m), 5.46(2H,s), 6.21(1H,brs), 7.20(2H,d,J=8.6Hz), 7.30-7.42(6H,m), 7.50-7.54(2H,m), 7.70(2H,s), 8.92(1H,brs), 9.39(1H,brs), 10.88-10.95(1H,m)
24	mp : 221-223℃ NMR δ: 2.90-3.08(3H,m), 3.10-3.22(3H,m), 4.04(2H,s), 4.97(1H,d,J=9.1Hz), 5.44(2H,s), 6.20(1H,brs), 7.20(2H,d,J=8.1Hz), 7.30-7.41(9H,m), 7.49(2H,d,J=8.6Hz), 7.55(2H,d,J=8.6Hz), 8.83(1H,brs), 9.16(1H,brs), 10.76(1H,s)
25	mp : 222-225℃ NMR δ: 2.60-3.05(3H,m), 3.10-3.20(3H,m), 4.43(2H,s), 5.01(1H,d,J=7.6Hz), 5.44(2H,s), 6.21(1H,brs), 7.15-7.23(4H,m), 7.26-7.46(5H,m), 7.51(2H,d,J=8.8Hz), 7.65-7.72(4H,m), 8.94(1H,brs), 9.41(1H,brs), 10.93(1H,s), 14.72(1H,brs)
26	mp : 197-203℃ NMR δ: 2.80-3.10(3H,m), 3.10-3.25(3H,m), 4.44(2H,s), 4.99(1H,d,J=8.0Hz), 5.61(2H,s), 6.21(1H,brs), 7.17(2H,d,J=8.6Hz), 7.30-7.42(5H,m), 7.48(2H,d,J=8.5Hz), 7.54(2H,d,J=8.0Hz), 7.70(2H,d,J=8.1Hz), 7.72-7.77(2H,m), 8.90(1H,brs), 9.34(1H,brs), 10.90(1H,s)
27	mp : 208-214℃ NMR δ: 2.90-3.10(3H,m), 3.10-3.22(3H,m), 4.44(2H,s), 4.97(1H,d,J=9.7Hz), 5.62(2H,s), 6.20(1H,brs), 7.16(2H,d,J=8.0Hz), 7.30-7.55(10H,m), 7.70-7.94(6H,m), 8.82(1H,brs), 9.14(1H,brs), 10.76(1H,s)
28	mp : 219-223℃ NMR δ: 2.11(3H.s), 2.92-3.08(3H,m), 3.10-3.20(3H,m), 4.43(2H,s), 5.02(1H,dd,J=10.2, 2.4Hz), 5.51(2H,s), 6.22(1H,brs), 7.14-7.34(7H,m), 7.36-7.42(4H,m), 7.48-7.53(3H,m), 8.95(1H,brs), 9.43(1H,brs), 10.94(1H,s), 14.61(1H,brs)

[0142]

[Table 17]

Ex.	D A T A
29	mp : 204-207℃ NMR δ: 2.24(3H.s), 2.80-3.10(3H,m), 3.10-3.50(3H,m), 4.43(2H,s), 5.01(1H,dd,J=10.3, 2.5Hz), 5.39(2H,s), 6.21(1H,brs), 7.17-7.24(2H,m), 7.30-7.42(7H,m), 7.47(2H,dd,J=8.8, 5.4Hz), 7.55(2H,d,J=8.3Hz), 8.94(1H,brs), 9.40(1H,brs), 11.00(1H,s), 14.70(1H,brs)
30	mp : 225-228℃ NMR δ: 2.90-3.07(3H,m), 3.10-3.23(3H,m), 4.28(2H,s), 4.97(1H,d,J=10.3Hz), 5.68(2H,s), 6.20(1H,d,J=3.4Hz), 7.16-7.23(4H,m), 7.30-7.46(7H,m), 7.53(2H,d,J=8.8Hz), 8.82(1H,brs), 9.11(1H,brs), 10.63(1H,s)
31	mp : 232-235℃ NMR δ: 2.90-3.10(3H,m), 3.10-3.25(3H,m), 4.03(2H,s), 4.98(1H,d,J=10.3Hz), 5.97(2H,s), 6.20(1H,brs), 7.19(2H,d,J=8.3Hz), 7.29-7.42(6H,m), 7.55(2H,d,J=8.3Hz), 7.67-7.77(2H,m), 8.87(1H,brs), 9.22(1H,brs), 10.49(1H,s), 14.61(1H,brs)
32	mp : 233-235℃ NMR δ: 2.90-3.10(3H,m), 3.10-3.25(3H,m), 4.01(2H,s), 4.98(1H,d,J=10.3Hz), 5.91(2H,s), 6.19(1H,brs), 7.17-7.48(11H,m), 7.55(2H,d,J=8.3Hz), 8.85(1H,brs), 9.18(1H,brs), 10.47(1H,s)
33	mp : 240-242℃ NMR δ: 2.90-3.10(3H,m), 3.10-3.25(3H,m), 4.32(2H,s), 4.98(1H,dt,J=10.3, 3.4Hz), 5.72(2H,s), 6.20(1H,d,J=3.9Hz), 7.20(2H,d,J=8.3Hz), 7.30-7.40(6H,m), 7.51(2H,d,J=8.8Hz), 7.62(1H,d,J=8.3Hz), 7.67(1H,d,J=2.0Hz), 8.86(1H,brs), 9.17(1H,brs), 10.67(1H,s)
34	mp : 221-224℃ NMR δ: 2.90-3.07(3H,m), 3.10-3.20(3H,m), 4.05(2H,s), 5.00(2H,dd,J=2.7, 10.2Hz), 7.21(2H,d,J=8.6Hz), 7.29-7.42(5H,m), 7.58(2H,d,J=8.6Hz), 8.83(1H,s), 8.91(1H,brs), 9.32(1H,brs), 10.62(1H,s)
35	mp : 222-224℃ NMR δ: 2.89-3.07(3H,m), 3.12-3.21(3H,m), 3.84(2H,s), 4.33(2H,s), 4.98(1H,dd,J=2.4, 10.2Hz), 7.20(2H,d,J=8.3Hz), 7.22-7.42(10H,m), 7.58(2H,d,J=8.3Hz), 8.87(1H,brs), 9.22(1H,brs), 10.44(1H,s)
36	mp : 242-245℃ NMR δ: 2.11(3H,s), 2.99-3.06(3H,m), 3.09-3.21(3H,m), 3.68(2H,s), 5.00(1H,dd,J=2.1, 10.2Hz), 6.02(1H,brs), 6.98(1H,s), 7.18(2H,d,J=8.1Hz), 7.28-7.42(5H,m), 7.58(2H,d,J=8.1Hz), 8.89(1H,brs), 9.30(1H,brs), 10.25(1H,s), 12.10(1H,s)
37	mp : 252-256℃ NMR δ: 2.89(3H,s), 2.91-3.07(3H,m), 3.11-3.21(3H,m), 3.65(2H,s), 4.95-5.02(1H,m), 6.20(1H,brs), 6.58(1H,s), 7.20(2H,d,J=8.6Hz), 7.28-7.42(5H,m), 7.57(2H,d,J=8.6Hz), 8.87(1H,brs), 9.24(1H,brs), 10.39(1H,s), 12.56(1H,s)

[0143]

[Table 18]

Ex.	D A T A
38	mp : >230℃(dec.) NMR δ: 2.88-3.22(6H,m), 3.73(2H,s), 3.65(2H,s), 5.00(1H,dd,J=2.0, 10.0Hz), 6.20(1H,brs), 7.12(1H,s), 7.18(2H,d,J=8.8Hz), 7.28-7.42(5H,m), 7.59(2H,d,J=8.8Hz), 8.39(4H,brs), 8.91(1H,brs), 9.32(1H,brs), 10.41(1H,s), 12.60(1H,s)
39	mp : 177-181℃ NMR δ: 2.90-3.10(3H,m), 3.10-3.25(3H,m), 3.67(2H,s), 5.00(1H,dd,J1=10.0, 2.0Hz), 6.68(1H,s), 6.97(1H,t,J=7.2Hz), 7.19(2H,d,J=8.4Hz), 7.27-7.42(9H,m), 7.59(2H,d,J=8.0Hz), 8.90(1H,brs), 9.29(1H,brs), 10.29(1H,s), 10.54(1H,brs)
40	mp : 237-243℃ NMR δ: 2.90-3.06(3H,m), 3.06-3.20(3H,m), 4.45(2H,s), 5.01(1H,dd,J=7.8, 2.0Hz), 5.70(2H,s), 6.21(1H,brs), 7.14(2H,d,J=8.8Hz), 7.29-7.42(5H,m), 7.46(2H,d,J=8.8Hz), 7.54(2H,d,J=8.8Hz), 7.77(2H,dd,J=14.4, 2.0Hz), 8.13(2H,d,J=8.4Hz), 8.94(1H,brs), 9.41(1H,brs), 10.95(1H,s)
41	mp : 151-159℃ NMR δ: 2.90-3.10(3H,m), 3.10-3.20(3H,m), 3.76(2H,s), 5.02(1H,dd,J=10.2, 2.7Hz), 6.70(1H,s), 7.20(2H,d,J=8.8Hz), 7.25-7.40(5H,m), 7.59(2H,d,J=8.8Hz), 8.96(1H,brs), 9.21(1H,brs), 9.43(1H,brs), 10.58(1H,s)
42	mp : 205-209℃ NMR δ: 2.90-3.08(3H,m), 3.13-3.23(3H,m),4.92-4.97(1H,m), 6.20(1H,brs), 7.19-7.42(10H,m), 7.71(2H,d,J=8.8Hz), 8.76(1H,brs), 8.92(1H,brs), 9.65(1H,s)
43	MS (m/z) : 411[(M+H)$^+$] NMR δ: 2.20(3H,s), 2.90-3.07(3H,m), 3.10-3.20(3H,m), 3.74(2H,s), 5.00(1H,dd,J=2.5, 10.3Hz), 7.20(2H,d,J=8.8Hz), 7.28-7.42(5H,m), 7.59(2H,d,J=8.8Hz), 8.91(1H,brs), 9.13(1H,brs), 9.33(1H,brs), 10.58(1H,s)
44	MS (m/z) : 425[(M+H)$^+$] NMR δ: 1.48(6H,s), 2.86-3.22(6H,m), 4.90-4.96(1H,m), 6.19(1H,brs), 6.40(1H.brs), 7.17(2H,d,J=8.8Hz), 7.27-7.41(5H,m), 7.56(2H,d,J=8.8Hz), 8.74(1H,brs), 8.90(1H,brs), 9.53(1H,brs)
45	MS (m/z) : 437[(M+H)$^+$] NMR δ: 1.68-2.12(4H,m), 2.43-2.59(2H,m), 2.91-3.07(3H,m), 3.11-3.20(3H,m), 3.76-3.81(1H,m), 5.00(1H,dd,J=2.5, 10.3Hz), 6.20(1H,brs), 7.19(2H,d,J=8.3Hz), 7.27-7.42(5H,m), 7.60(1H,d,J=8.3Hz), 8.90(1H,brs), 9.33(1H,brs), 10.43(1H,s)
46	MS (m/z) : 421 [(M+H)$^+$] NMR δ: 2.88-3.24(6H,m), 3.83(2H,s), 4.95-5.04(1H,m), 6.19(1H,brs), 7.16-7.22(2H,m), 7.26-7.45(6H,m), 7.55-7.63(2H,m), 7.87(1H,s), 8.04(1H,d,J=3.6Hz), 8.91(1H,brs), 9.32(1H,brs), 10.42(1H,brs)
47	MS (m/z) : 456[(M+H)$^+$] NMR δ: 2.84-3.19(6H,m), 4.03(2H,s), 4.87-4.97(1H,m), 5.43(2H,s), 6.12(2H,s), 7.20(2H,d,J=8.3Hz), 7.25-7.41(11H,m), 7.53(2H,d,J=8.3Hz), 7.90(1H,s), 10.38(1H,s)

[0144]

[Table 19]

Ex.	D A T A
48	MS (m/z) : 456[(M+H)$^+$] NMR δ: 2.88-3.18(6H,m), 3.69(2H,s), 4.87-4.95(1H,m), 5.36(2H,s), 6.15-6.21(1H,m), 7.18(2H,d,J=8.3Hz), 7.27-7.41(11H,m), 7.54(2H,d,J=8.3Hz), 8.57(1H,s), 8.72(1H,brs), 8.82(1H,brs), 10.20(1H,s)
49	MS (m/z) : 504[(M+H) $^+$] NMR δ: 2.88-3.07(3H,m), 3.11-3.21(3H,m), 3.67(2H,s), 4.93-4.99(1H,m), 5.53(2H,s), 6.20(1H,d,J=3.9Hz), 7.00(1H,s), 7.13(2H,d,J=7.3Hz), 7.18(2H,d,J=8.3Hz), 7.24-7.42(8H,m), 7.49(2H,d,J=8.3Hz), 8.82(1H,brs), 9.11(1H,brs), 10.35(1H,s)
50	MS (m/z) : 416 [(M+H)$^+$] NMR δ: 1.76-1.87(2H,m), 2.18-2.26(2H,m), 2.80-3.22(8H,m), 4.39-4.47(1H,m), 4.95-5.07(1H,m), 7.15-7.22(2H,m), 7.27-7.43(5H,m), 7.54-7.63(2H,m), 7.74-7.82(1H,m), 8.27(1H,d,J=7.2Hz), 8.67(1H,d,J=4.8Hz), 8.97(1H,brs), 9.47(1H,brs), 10.74(1H,brs)
51	MS (m/z) : 441[(M+H)$^+$] NMR δ: 2.90-3.10(3H,m), 3.10-3.20(3H,m), 4.18(2H,s), 4.96(1H,d,J=8.0Hz), 6.20(1H,brs), 7.18(2H,d,J=8.6Hz), 7.20-7.60(12H,m), 7.84(1H,s), 7.97(1H,s), 8.83(1H,brs), 9.17(1H,brs), 10.55(1H,s)
52	MS (m/z) : 497[(M+H)$^+$] NMR δ: 1.14(6H,d,J=12.9Hz), 2.83(1H,sep,J=12.9Hz), 2.90-3.22(6H,m), 4.38(2H,s), 4.97(1H,d,J=4.1Hz), 5.39(2H,s), 6.20(1H,brs), 7.07-7.42(10H,m), 7.52(2H,d,J=8.8Hz), 7.67(2H,d,J=3.9Hz), 8.84(1H,brs), 9.17(1H,brs), 10.76(1H,s)
53	MS (m/z) : 497[(M+H)$^+$] NMR δ: 1.14(6H,d,J=12.9Hz), 2.83(1H,sep,J=12.9Hz), 2.90-3.22(6H,m), 4.38(2H,s), 4.97(1H,d,J=4.1Hz), 5.39(2H,s), 6.20(1H,brs), 7.07-7.42(10H,m), 7.52(2H,d,J=8.8Hz), 7.67(2H,d,J=3.9Hz), 8.84(1H,brs), 9.17(1H,brs), 10.76(1H,s)
54	MS (m/z) : 489[M$^+$] NMR δ: 2.95-3.02(3H,m), 3.15(3H,brs), 4.44(2H,s), 5.01(1H,dd,J=10.3, 2.5Hz), 5.58(2H,s), 6.21(1H,brs), 7.19(2H,d,J=8.6Hz), 7.27-7.42(6H,m), 7.51(2H,d,J=8.6Hz), 7.58-7.60(1H,m), 7.69(1H,d,J=2.4Hz), 7.72(1H,d,J=2.0Hz), 7.75(1H,d,J=2.0Hz), 8.96(1H,brs), 9.44(1H,brs), 10.91(1H,s)
55	MS (m/z) : 489[M$^+$] NMR δ: 2.94-3.04(3H,m), 3.15(3H,brs), 3.94(2H,s), 5.01(1H,d,J=10.3Hz), 5.31(2H,s), 6.21(1H,d,J=3.9Hz), 7.01(1H,s), 7.17-7.41(12H,m), 7.54(2H,d,J=8.3Hz), 8.98(1H,brs), 9.35(1H,brs), 10.55(1H,s)
56	MS (m/z) : 523[M$^+$] NMR δ: 2.95-3.05(3H,m), 3.15(3H,brs), 4.44(2H,s), 5.01(1H,dd,J=10.3, 2.5Hz), 5.51(2H,s), 6.20(1H,brs), 7.19(3H,d,J=8.6Hz), 7.26-7.42(7H,m), 7.50-7.54(3H,m), 7.58(1H,d,J=2.0Hz), 7.73(1H,d,J=2.0Hz), 8.95(1H,brs), 9.43(1H,brs), 10.98(1H,s)

[0145]

[Table 20]

Ex.	D A T A
57	MS (m/z) : 456[(M+H)$^+$] NMR δ: 2.92-3.05(3H,m), 3.15(3H,brs), 4.43(2H,s), 5.01(1H,dd,J=10.2, 2.6 Hz), 5.65(2H,s), 7.20(2H,d,J=8.4Hz), 7.29-7.48(5H,m), 7.50-7.53(3H,m), 7.70(1H,d,J=2.0Hz), 7.78(1H,d,J=2.0Hz), 7.85(1H,dt,J=8.0, 2.0Hz), 8.49(1H,d,J=8.0Hz), 8.94(1H,brs), 9.42(1H,brs), 10.86(1H,s)
58	mp : 150-152°C NMR δ: 2.88-3.07(3H,m), 3.08(3H,m), 3.95(2H,s), 5.00(1H,dd,J=2.8, 10.0 Hz), 6.21(1H,s), 6.82(1H,d,J=7.6Hz), 6.91(1H,d,J=8.0Hz), 7.17-7.23(2H,m), 7.28-7.43(5H,m), 7.55-7.62(2H,m), 7.82-8.04(3H,m), 8.90(1H,brs), 9.31(1H,brs), 10.67(1H,brs), 14.07(1H,brs)
59	MS (m/z) : 413 [(M+H)$^+$] NMR δ: 2.90-3.25(6H,m), 4.95-5.04(1H,m), 5.20(1H,s), 6.22(1H,brs), 6.78(1H,s), 7.17-7.24(2H,m), 7.27-7.44(5H,m), 7.67-7.75(2H,m), 8.50-9.10(3H,br), 9.45(1H,br), 10.22(1H,brs)
60	mp : 214-216°C NMR δ: 2.86-3.24(6H,m), 3.65(2H,s), 4.98(1H,dd,J=2.8, 10.4Hz), 6.18(1H,d,J=6.8Hz), 6.28 (1H,d,J=8.8Hz), 7.16-7.22(2H,m), 7.28-7.45(6H,m), 7.53-7.59(2H,s), 8.85(1H,brs), 9.18 (1H,brs), 10.36(1H,brs)
61	mp : 180-182°C NMR δ: 0.87(6H,d,J=6.8Hz), 2.05-2.15(1H,m), 2.59-3.10(3H,m), 3.10-3.20(3H,m), 4.03(2H,d,J=7.8Hz), 4.41(2H,s), 5.01(1H,d,J=8.3Hz), 6.20(1H,brs), 7.21(2H,d,J=8.3Hz), 7.29-7.42(9H,m), 7.60(2H,d,J=8.8Hz), 7.69(1H,d,J=1.9 Hz), 7.75(1H,d,J=2.0Hz)
62	mp : 226-228°C NMR δ: 2.87-3.23(6H,m), 4.45(2H,s), 5.02(1H,dd,J=2.4, 10.0Hz), 5.55(2H,s), 6.21(1H,brs), 7.16-7.46(11H,m), 7.49-7.55(2H,m), 7.66(1H,d,J=2.0Hz), 7.71(1H,d,J=2.0Hz), 8.95(1H,brs), 9.44(1H,brs), 10.93(1H,brs), 14.82(1H,brs)
63	mp : 224-225°C NMR δ: 2.90-3.05(3H,m), 3.05-3.25(3H,m), 4.46(2H,s), 5.01(1H,d,J=8.0Hz), 5.50(2H,s), 6.21(1H,brs), 7.14-7.50(11H,m), 7.54(2H,d,J=8.8Hz), 7.70-7.73(2H,m), 8.93(1H,brs), 9.39(1H,brs), 10.95(1H,s)
64	mp : 205-208°C NMR δ: 2.90-3.06(3H,m), 3.10-3.21(3H,m), 4.41(2H,s), 4.99(1H,d,J=8.3Hz), 5.51(2H,s), 6.21(1H,s), 7.06-7.12(1H,m), 7.20(2H,d,J=8.3Hz), 7.28-7.42(6H,m), 7.69(2H,dd,J=2.0, 8.3Hz), 8.87(1H,s), 9.26(1H,s), 10.81(1H,s)
65	mp : 211-216°C NMR δ: 3.00(3H,brs), 3.15(3H,brs), 4.44(2H,s), 5.05(1H,dd,J=10.2, 1.9Hz), 5.58(2H,s), 6.22(1H,brs), 7.14-7.22(4H,m), 7.29-7.32(1H,m), 7.37-7.42(4H,m), 7.47-7.54(3H,m), 7.65(1H,s), 7.69(1H,d,J=1.9Hz), 9.02(1H,brs), 9.55(1H,brs), 10.97(1H,s)

[0146]

[Table 21]

Ex.	D A T A
66	mp : 199-201℃ NMR δ: 2.87-3.23(6H,m), 4.45(2H,s), 4.95-5.04(1H,m), 5.51(2H,s), 6.20(1H,brs), 7.10-7.43(10H,m), 7.49-7.55(2H,m), 7.71(1H,d,J=2.0Hz), 7.74(1H,d,J=2.0Hz), 8.89(1H,brs), 9.30(1H,brs), 10.90(1H,brs), 14.73(1H,brs)
67	mp : 131-135℃ NMR δ: 3.00(3H,brs), 3.16(3H,brs), 4.49(2H,s), 5.04(1H,d,J=10.0Hz), 5.56(2H,s), 6.23(1H,brs), 7.20(2H,d,J=8.2Hz), 7.23-7.34(4H,m), 7.37-7.42(4H,m), 7.53(2H,d,J=8.2Hz), 7.72(2H,s), 9.01(1H,brs), 9.54(1H,brs), 11.00(1H,s)
68	mp : 217-219℃ NMR δ: 2.90-3.05(3H,m), 3.05-3.20(3H,m), 4.46(2H,s), 5.00(1H,d,J=8.0Hz), 5.47(2H,s), 6.21(1H,brs), 7.20(2H,d,J=8.0Hz), 7.25-7.50(7H,m), 7.50-7.60(3H,m), 7.70(1H,d,J=1.9Hz), 7.71(1H,d,J=2.0Hz), 8.91(1H,brs), 9.33(1H,brs), 10.93(1H,s)
69	mp : 213-217℃ NMR δ: 2.90-3.05(3H,m), 3.05-3.20(3H,m), 4.42(2H,s), 5.02(1H,dd,J=10.2, 2.4Hz), 5.62(2H,s), 6.21(1H,brs), 7.20(2H,d,J=8.3Hz), 7.29-7.42(6H,m), 7.49(2H,d,J=8.3Hz), 7.51-7.60(1H,m), 7.68-7.73(2H,m), 8.95(1H,brs), 9.42(1H,brs), 10.89(1H,s)
70	mp : 212-213℃ NMR δ: 2.87-3.23(6H,m), 4.47(2H,s), 5.02(1H,dd,J=2.4, 10.0Hz), 5.53(2H,s), 6.21(1H,brs), 7.16-7.23(2H,m), 7.28-7.34(1H,m), 7.36-7.43(4H,m), 7.48-7.55(2H,m), 7.57-7.67(2H,m), 7.69-7.74(2H,m), 8.95(1H,brs), 9.43(1H,brs), 10.95(1H,brs), 14.86(1H,brs)
71	mp : 209-213℃ NMR δ: 2.90-3.05(3H,m), 3.05-3.20(3H,m), 4.47(2H,s), 4.98-5.01(1H,m), 5.49(2H,s), 6.21(1H,brs), 7.21(2H,d,J=8.3Hz), 7.28-7.34(1H,m), 7.36-7.44(6H,m), 7.53(2H,d,J=8.8Hz), 7.71(1H,d,J=1.9Hz), 7.74(1H,d,J=1.9Hz), 8.91(1H,brs), 9.34(1H,brs), 10.97(1H,s)
72	mp : 190-193℃ NMR δ: 2.90-3.08(3H,m), 3.10-3.21(3H,m), 4.38(2H,s), 4.99(1H,dd,J=2.5, 10.2Hz), 5.69(2H,s), 6.20(1H,s), 7.21(2H,d,J=8.8Hz), 7.29-7.42(5H,m), 7.48(2H,d,J=8.3Hz), 7.70(1H,d,J=1.9Hz), 7.77(1H,s), 8.88(1H,s), 9.27(1H,s), 10.84(1H,s)
73	mp : 233-234℃ NMR δ: 2.90-3.23(6H,m), 4.47(2H,s), 5.02(1H,dd,J=2.4, 10.0Hz), 5.44(2H,s), 6.21(1H,brs), 7.12-7.23(3H,m), 7.28-7.34(1H,m), 7.36-7.44(5H,m), 7.52-7.58(2H,m), 7.66-7.73(3H,m), 7.79-7.81(1H,m), 8.96(1H,brs), 9.44(1H,brs), 10.96(1H,brs), 14.79(1H,brs)
74	mp : 180-183℃ NMR δ: 2.67-2.76(4H,m), 2.78-2.86(2H,m), 4.00(2H,s), 4.66(1H,dd,J=8.3, 3.9Hz), 5.39(2H,s), 5.42(1H,brs), 6.57(1H,d,J=0.9Hz), 6.78(1H,s), 7.03(2H,d,J=8.3Hz), 7.21-7.26(1H,m), 7.27-7.34(4H,m), 7.46-7.50(1H,m), 7.52(2H,d,J=8.3Hz), 7.56(1H,s), 7.58(1H,s), 8.32(1H,s), 10.32(1H,s)

[0147]

[Table 22]

Ex.	D A T A
75	mp : 210-215°C NMR δ: 2.91-3.03(3H,m), 3.15(3H,brs), 4.44(2H,s), 5.01(1H,dd,J=10.4, 2.6 Hz), 5.53(2H,s), 6.21(1H,brs), 7.18(2H,d,J=8.3Hz), 7.30-7.32(1H,m), 7.37-7.42(4H,m), 7.48(2H,d,J=8.3Hz), 7.49(2H,d,J=8.3Hz), 7.74(1H,d,J=2.0Hz), 7.75(1H,d,J=2.0Hz), 7.79(2H,d,J=8.3Hz), 8.94(1H,brs), 9.39(1H,brs), 10.93 (1H,s)
76	mp : 162-165°C NMR δ: 2.93-3.05(3H,m), 3.14(3H,brs), 4.47(2H,s), 5.03(1H,dd,J=10.3, 2.5 Hz), 5.62(1H,brs), 5.89(2H,s), 7.12(2H,d,J=8.3Hz), 7.30-7.37(1H,m), 7.39-7.43(6H,m), 7.61(2H,d,J=8.8Hz), 7.69(1H,t,J=7.5Hz), 7.75(1H,d,J=1.9Hz), 7.83-7.86(2H,m), 7.97(1H,d,J=8.3Hz), 8.44(1H,d,J=8.3Hz), 8.99(1H,brs), 9. 52(1H,brs), 10.84(1H,s)
77	MS (m/z) : 507[M^+] NMR δ: 2.64-2.74(4H,m), 2.77-2.82(2H,m), 3.93(2H,s), 4.63(1H,dd,J=7.8, 4.4Hz), 5.33(2H,s), 6.80(2H,d,J=6.3Hz), 7.14(2H,d,J=8.8Hz), 7.20-7.24(1H, m), 7.28-7.35(5H,m), 7.43(1H,d,J=7.8Hz), 7.47-7.52(3H,m), 10.27(1H,s)
78	MS (m/z) : 507[M^+] NMR δ: 2.63-2.72(4H,m), 2.75-2.81(2H,m), 3.79(2H,s), 4.62(1H,dd,J=7.8, 4.4Hz), 5.30(1H,brs), 5.33(2H,s), 6.68(1H,d,J=1.0Hz), 6.91(1H,dd,J=8.8, 5. 9Hz), 7.06(1H,d,J=1.0Hz), 7.12(2H,d,J=8.8Hz), 7.19-7.24(2H,m), 7.28-7.33 (4H,m), 7.43(2H,d,J=8.3Hz), 7.49(1H,dd,J=8.3, 2.5Hz), 8.32(1H,s), 10.21(1 H,s)
79	MS (m/z) : 523 [$(M+H)^+$] NMR δ: 2.88-3.08(3H,m), 3.10-3.22(3H,m), 4.40(2H,s), 4.97(1H,d,J=8.3Hz) , 5.56(2H,s), 6.20(1H,s), 7.19(2H,d,J=8.3Hz), 7.24(1H,d,J=2.5Hz), 7.30-7.6 0(9H,m), 7.64(1H,d,J=2.0Hz), 7.72(1H,s), 8.83(1H,s), 9.14(1H,s), 10.71(1H ,s)
80	MS (m/z) : 509 [$(M+H)^+$] NMR δ: 2.90-3.08(3H,m), 3.10-3.22(3H,m), 4.44(2H,s), 5.02(1H,d,J=8.8Hz) , 5.59(2H,s), 6.21(1H,s), 7.20(2H,d,J=8.0Hz), 7.24-7.42(7H,m), 7.50(2H,d,J =8.8Hz), 7.72(2H,d,J=6.8Hz), 8.94(1H,s), 9.42(1H,s), 10.93(1H,s)
81	MS (m/z) : 513 [$(M+H)^+$] NMR δ: 2.87-3.23(6H,m), 3.85(3H,s), 4.30(2H,s), 4.94-5.01(1H,m), 5.55(2 H,s), 6.17-6.22(1H,br), 7.14-7.23(2H,m), 7.28-7.50(9H,m), 7.57-7.64(2H,m), 7.87-7.93(2H,m), 8.83(1H,brs), 9.10(1H,brs), 10.68(1H,brs), 14.86(1H,brs)
82	MS (m/z) : 566 [$(M+H)^+$] NMR δ: 1.30-1.64(6H,m), 2.88-3.22(8H,m), 3.45-3.65(2H,m), 4.39(2H,s), 4 .97(1H,d,J=9.8Hz), 5.50(2H,s), 6.21(1H,s), 7.20(2H,d,J=8.3Hz), 7.30-7.42(9H,m), 7.51(2H,d,J=8.7Hz), 7.71(2H,d,J=7.8Hz), 8.81(1H,s), 9.14(1H,s), 1 0.77(1H,s)

[0148]

[Table 23]

Ex.	D A T A
83	mp : 229-232℃ NMR δ: 2.90-3.00(3H,m), 3.10-3.18(3H,m), 5.00(1H,dd,J=2.8, 10.1Hz), 5.03(2H,s), 6.27(1H,t,J=2.0Hz), 7.20(2H,d,J=8.8Hz), 7.29-7.42(5H,m), 7.46(1H,d,J=2.4Hz), 7.58(2H,d,J=8.8Hz), 7.77(1H,d,J=2.0Hz), 8.91(1H,s), 9.32(1H,s), 10.53(1H,s)
84	mp : 237-240℃ NMR δ: 2.90-3.08(3H,m), 3.10-3.22(3H,m), 4.96(1H,dd,J=2.0, 10.0Hz), 5.15(2H,s), 7.21(2H,d,J=8.0Hz), 7.28-7.42(5H,m), 7.56(2H,d,J=8.4Hz), 8.03(1H,s), 8.61(1H,s), 8.82(1H,s), 9.09(1H,s), 10.57(1H,s)
85	mp : 244-248℃ NMR δ: 2.90-3.06(3H,m), 3.10-3.20(3H,m), 5.00(1H,d,J=7.6Hz), 5.20(2H,s), 6.20(1H,s), 7.20-7.50(11H,m), 7.59(2H,d,J=7.2Hz), 8.94(3H,s), 9.36(1H,s), 10.95(1H,s), 12.92(1H,s)
86	mp : 223-224℃ NMR δ: 2.86-3.22(6H,m), 3.49(2H,s), 4.93-5.03(1H,m), 6.20(1H,d,J=4.0Hz), 7.15-7.43(9H,m), 7.55-7.62(2H,m), 7.75(1H,dt,J=1.6, 8.0Hz), 8.45-8.53(1H,m), 8.06-9.50(2H,br), 10.35(1H,brs)
87	mp : 236-238℃ NMR δ: 2.86-3.23(6H,m), 3.72(2H,s), 4.91-5.02(1H,m), 6.20(1H,d,J=4.0Hz), 7.15-7.22(2H,m), 7.27-7.45(6H,m), 7.53-7.62(2H,m), 7.73-7.82(1H,m), 8.40-8.60(2H,m), 8.84(1H,brs), 9.16(1H,brs), 10.35-10.50(1H,br)
88	mp : 195-198℃ NMR δ: 2.86-3.22(6H,m), 3.73(2H,s), 4.93-5.04(1H,m), 6.15-6.25(1H,br), 7.14-7.22(2H,m), 7.28-7.43(7H,m), 7.54-7.63(2H,m), 8.47-8.53(2H,m), 9.07(2H,brs), 10.50(1H,brs)
89	mp : 202-204℃ NMR δ: 2.71-2.81(2H,m), 2.88-3.24(8H,m), 3.49(2H,s), 4.93-5.05(1H,m), 6.20(1H,brd,J=3.2Hz), 7.15-7.23(3H,m), 7.26-7.44(6H,m), 7.52-7.60(2H,m), 7.69(1H,dt,J=1.6, 7.6Hz), 8.45-8.51(1H,m), 9.07(2H,brs), 10.07(1H,brs)
90	mp : 220-227℃ NMR δ: 2.80-3.20(8H,m), 4.31(2H,s), 4.42(2H,t,J=8.0Hz), 5.00(1H,d,J=1.0Hz), 6.21(1H,brs), 7.20-7.40(12H,m), 7.59(2H,d,J=8.6Hz), 7.65(2H,dd,J=12.9, 0.9Hz), 8.91(1H,brs), 9.34(1H,brs), 10.98(1H,s)
91	mp : 158-165℃ NMR δ: 2.51-2.78(6H,m), 3.96(2H,s), 4.59(1H,t,J=5.2Hz), 5.20(1H,brs), 7.13-7.32(9H,m), 7.50-7.53(4H,m), 10.33(1H,s), 12.37(1H,brs)
92	mp : 216-217℃ NMR δ: 2.31(3H,s), 2.86-3.24(6H,m), 3.89(2H,s), 4.92-5.07(1H,m), 6.20(1H,d,J=4.0Hz), 7.12-7.22(3H,m), 7.28-7.45(5H,m), 7.50-7.64(2H,m), 8.30(1H,d,J=4.4Hz), 8.60-9.50(2H,br), 10.32(1H,brs)

[0149]

[Table 24]

Ex.	D A T A
93	mp : 236-238℃ NMR δ: 2.86-3.24(6H,m), 3.95(2H,s), 4.91-5.01(1H,m), 5.44(2H,s), 6.19(1H,d,J=4.4Hz), 7.15-7.22(2H,m), 7.27-7.43(5H,m), 7.52-7.62(2H,m), 8.50-8.69(3H,m), 8.83(1H,br), 9.12(1H,brs), 10.41(1H,brs)
94	MS (m/z) : 455[(M+H)$^+$] NMR δ: 2.90-3.10(3H,m), 3.10-3.20(3H,m), 4.38(2H,s), 4.98(1H,t,J=10.4Hz), 5.44(2H,s), 6.20(1H,d,J=3.2Hz), 7.20(2H,d,J=8.4Hz), 7.30-7.45(9H,m), 7.53(2H,d,J=8.8Hz), 7.64(2H,s), 8.85(1H,brs), 9.21(1H,brs), 10.79(1H,s)
95	MS (m/z) : 390[(M+H)$^+$] NMR δ: 2.31(3H,s), 2.89-3.17(6H,m), 3.79(2H,s), 4.98(1H,dt,J=3.2, 10.4Hz), 7.10-7.41(12H,m), 10.32(1H,s)
96	MS (m/z) : 390[(M+H)$^+$] NMR δ: 2.27(3H,s), 2.89-3.17(6H,m), 3.79(2H,s), 4.99(1H,dt,J=3.6, 10.0Hz), 7.17-7.59(12H,m), 10.31(1H,s)
97	MS (m/z) : 390[(M+H)$^+$] NMR δ: 2.44(3H,s), 2.78-3.20(6H,m), 3.80(2H,s), 4.97(1H,dt,J=3.2, 10.4Hz), 7.12-7.66(12H,m), 10.33(1H,s)
98	MS (m/z) : 513 [(M+H)$^+$] NMR δ: 1.06(3H,d,J=6.4Hz), 2.50-2.65(2H,m), 2.90-3.15(3H,m), 3.83(2H,s), 4.80-4.94(1H,m), 7.10-7.18(2H,m), 7.23-7.45(7H,m), 7.52-7.60(2H,m), 7.71-7.80(1H,m), 8.41-8.52(1H,m), 10.25(1H,brs)
99	mp : 203-204℃ NMR δ: 1.13(3H,d,J=6.4Hz), 2.55-2.64(1H,m), 3.00-3.50(4H,m), 3.84(2H,s), 4.92-5.02(1H,m), 6.20(1H,d,J=4.0Hz), 7.13-7.20(2H,m), 7.24-7.46(7H,m), 7.54-7.60(2H,m), 7.73-7.80(1H,m), 8.51(1H,brs), 8.67(1H,brs), 9.13(1H,brs), 10.31(1H,brs)
100	MS (m/z) : 513 [(M+H)$^+$] NMR δ: 1.06(3H,d,J=6.4Hz), 2.50-2.65(1H,m), 2.57-3.50(4H,m), 3.78(2H,s), 4.77-4.92(1H,m), 5.25(2H,s), 6.85(1H,s), 7.10-7.55(15H,m), 10.33(1H,brs)
101	mp : 194-196℃ NMR δ: 2.88-3.25(6H,m), 3.89(2H,s), 5.20-5.26(1H,m), 6.30(1H,s), 7.17-7.48(7H,m), 7.54-7.60(3H,m), 7.81-7.88(1H,m), 8.54(1H,d,J=4.0Hz), 8.82(1H,s), 9.16(1H,s), 10.35(1H,s)
102	mp : 214-215℃ NMR δ: 2.88-3.25(6H,m), 3.85(2H,s), 4.96-5.02(1H,m), 6.33(1H,d,J=3.8Hz), 7.12-7.31(6H,m), 7.39-7.48(2H,m), 7.58(2H,d,J=8.3Hz), 7.74-7.80(1H,m), 8.50(1H,s), 8.82(1H,s), 9.01(1H,s), 10.30(1H,s)
103	mp : 223-225℃ NMR δ: 2.88-3.06(3H,m), 3.10-3.20(3H,m), 3.84(2H,s), 4.94-5.01(1H,m), 6.24(1H,d,J=4.0Hz), 7.16-7.30(5H,m), 7.38-7.46(3H,m), 7.58(2H,d,J=8.8Hz), 7.76(1H,dt,J=1.6, 7.6Hz), 8.50(1H,d,J=8.8Hz), 8.83(1H,s), 9.08(1H,s), 10.31(1H,s)

[0150]

[Table 25]

Ex.	D A T A
104	mp : 208-210℃ NMR δ: 2.88-3.24(6H,m), 3.99(2H,s), 4.90-5.01(1H,m), 6.20(1H,d,J=3.6Hz), 7.15-7.24(2H,m), 7.28-7.44(6H,m), 7.53-7.62(2H,m), 8.50-9.30(4H,m), 10.33(1H,brs)
105	mp : 234-235℃ NMR δ: 2.94-3.25(6H,m), 4.07(2H,s), 4.90-5.02(1H,m), 6.20(1H,d,J=4.0Hz), 7.16-7.23(2H,m), 7.27-7.44(5H,m), 7.53-7.65(4H,m), 7.71-7.78(1H,m), 7.94-8.00(2H,m), 8.33(1H,d,J=8.0Hz), 8.50-9.25(2H,m), 10.46(1H,brs)
106	mp : 221-222℃ NMR δ: 2.90-3.25(6H,m), 3.85(2H,s), 4.92-5.08(1H,m), 6.35(1H,d,J=3.6Hz), 7.14-7.23(2H,m), 7.23-7.31(1H,m), 7.33-7.50(5H,m), 7.54-7.64(2H,m), 7.76(1H,dt,J=1.6, 7.6Hz), 8.43-8.55(1H,m), 8.80-9.40(2H,br), 10.36(1H,brs)
107	mp : 204-205℃ NMR δ: 2.85-3.28(6H,m), 3.85(2H,s), 5.02-5.14(1H,m), 6.37(1H,d,J=4.0Hz), 7.14-7.32(3H,m), 7.36-7.46(2H,m), 7.55-7.64(2H,m), 7.70-7.86(2H,m), 8.46-8.56(2H,m), 8.57-8.65(1H,m), 9.13(2H,brs), 10.37(1H,brs)
108	MS (m/z) : 539[M^+] NMR δ: 2.63-2.67(4H,m), 2.73-2.78(2H,m), 4.07(2H,s), 4.60(1H,dd,J=7.4, 4.9Hz), 5.24(1H,brs), 5.57(2H,s), 7.12-7.23(7H,m), 7.27-7.31(4H,m), 7.37(3H,d,J=8.3Hz), 7.46(2H,d,J=8.3Hz), 7.60-7.61(1H,m), 8.31(1H,s), 10.31(1H,s)
109	MS (m/z) : 404[$(M+H)^+$] NMR δ: 2.26(3H,s), 2.40(3H,s), 2.90-3.17(6H,m), 3.75(2H,s), 4.99(1H,dt,J=3.2, 6.8Hz), 6.97-7.60(11H,m), 10.35(1H,s)
110	mp : 183-184℃ NMR δ: 1.85-2.05(2H,m), 2.53-2.65(2H,m), 2.83-3.03(3H,m), 3.05-3.16(1H,m), 3.88(2H,s), 4.95(1H,d,J=9.6Hz), 6.15(1H,brs), 7.10-7.18(2H,m), 7.22-7.43 (7H,m), 7.50-7.60(2H,m), 7.75(1H,dt,J=1.6, 7.2Hz), 8.45-8.53(1H,m), 8.91(2H,brs), 10.29(1H,brs)
111	mp : 225-226℃ NMR δ: 3.02-3.14(1H,m), 3.18-3.46(3H,m), 3.84(2H,s), 4.22-4.35(2H,m), 4.98-5.08(1H,m), 6.21(1H,d,J=3.6Hz), 6.90-6.97(2H,m), 7.23-7.44(7H,m), 7.53-7.62(2H,m), 7.76(1H,dt,J=1.6, 7.2Hz), 8.45-8.54(1H,m), 8.80-9.50(2H,br), 10.29(1H,brs)
112	MS (m/z) : 404 [$(M+H)^+$] NMR δ: 1.21(6H,s), 2.85-3.23(4H,m), 3.89(2H,s), 4.90-5.00(1H,m), 6.21(1H,brs), 7.11-7.19(2H,m), 7.28-7.50(7H,m), 7.53-7.62(2H,m), 7.78-7.90(1H,m), 8.45-8.60(2H,m), 9.00-9.10(1H,br), 10.35(1H,brs)
113	mp : 132-133℃ NMR δ: 2.90-3.10(3H,m), 3.13-3.23(3H,m), 4.96(1H,dd,J=2.5, 10.2Hz), 7.06-7.11(1H,m,), 7.21(2H,d,J=8.7Hz), 7.30-7.42(5H,m), 7.47-7.53(3H,m), 7.81-7.87(1H,m), 8.29(1H,d,J=4.9Hz), 8.78(1H,s), 9.00(1H,s), 9.88(1H,s), 10.51(1H,s)

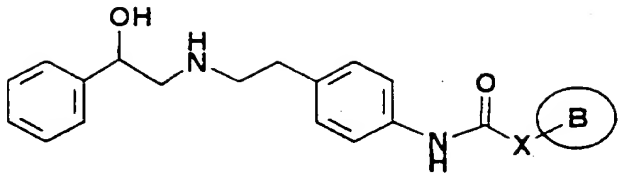
[0151]

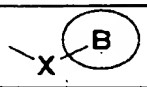
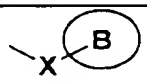
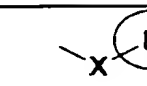
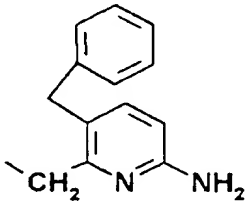
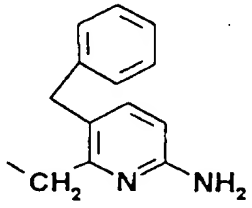
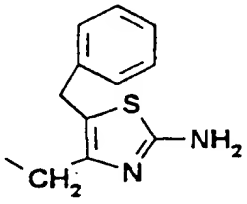
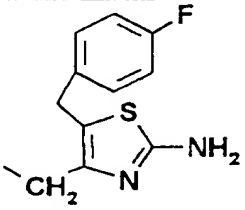
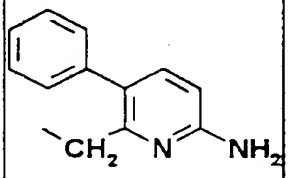
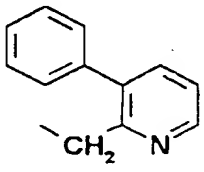
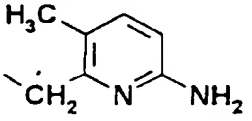
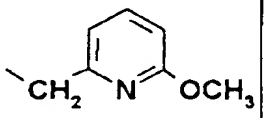
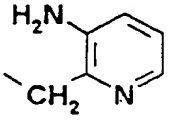
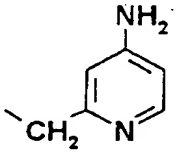
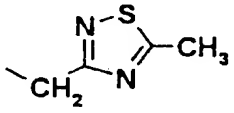
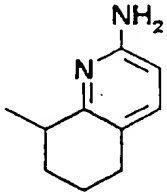
The compounds shown in Tables 26 and 27 together with chemical structural formulae can be easily manufactured by almost the same method as mentioned in the above Examples or Manufacturing Methods or by the method to which some modifications known to the persons skilled in the art are applied.

Incidentally, in some cases, there are tautomeric, geometric or optical isomers for the compounds mentioned in Tables 26 and 27, and the compounds of the present invention cover each of the isolated isomers of the above-mentioned ones or a mixture thereof.

[0152]

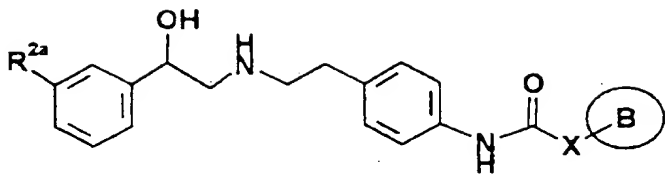
[Table 26]

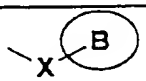
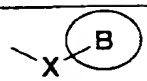
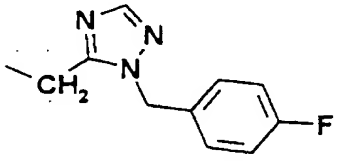
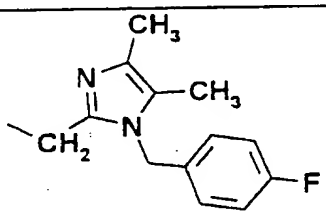
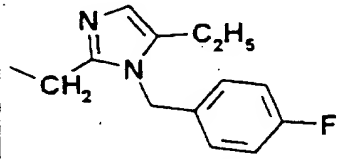
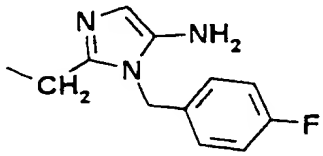
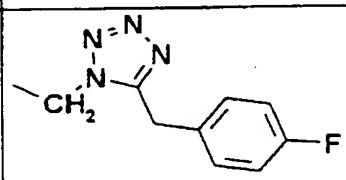
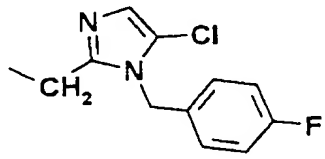
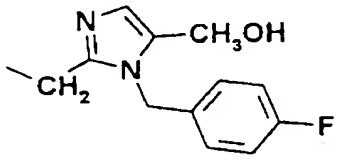
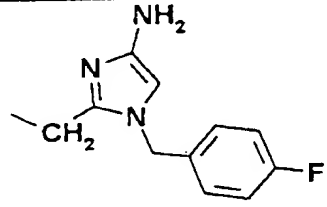
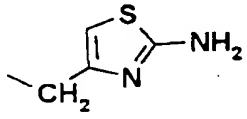
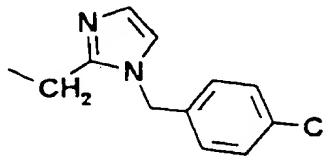


No.		No.		No.	
1		2		3	
4		5		6	
7		8		9	
10		11		12	

[0153]

[Table 27]



No.	R^{2a}		No.	R^{2a}	
13	H		14	H	
15	H		16	H	
17	H		18	H	
19	H		20	H	
21	Cl		22	Cl	

[Document Name] Abstract

[Abstract]

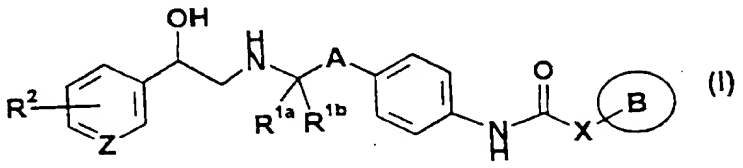
[Matters to be Solved]

Creation of a therapeutic agent for diabetes mellitus having both an insulin secretion promoting action and an insulin sensitivity potentiating action and also having a selective stimulating action to β_3-receptors

[Means to Solve the Matters]

An amide derivative represented by the following formula:

[Formula 1]



(I)

(In the above formula, each of the symbols means as follows:

ring B: a nitrogen-containing heteroaryl group which may be substituted and may be fused with a benzene ring;

X: a bond, an optionally hydroxy- or lower alkyl-substituted linear lower alkylene, lower alkenylene or carbonyl, or a group represented by a formula -NH- (when X is a linear lower alkylene group which may be substituted with a lower alkyl group, the hydrogen atom bonded to the carbon atom constituting a ring B may form a lower alkylene group together with the lower alkyl group so that a ring is formed);

A: methylene, ethylene or a group represented by a formula $-CH_2O-$;

R^{1a}, R^{1b}: they may be same or different and each is a hydrogen atom or a lower alkyl group;

R^2: a hydrogen atom or a halogen atom; and

Z: a nitrogen atom or a group represented by a formula =CH-)

or a salt thereof.

[Selective Drawing] No